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PRIMARY, SOLITARY LYMPHOID TUMORS OF THE GASTRO-INTESTINAL TRACT

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THE DISTINCTION between local and generalized forms of lymphoid growths is not widely recognized. In the present communication we propose to discuss the primary, solitary lymphoid tumors of the gastro-intestinal tract.*

The publication within the last few years of studies^{1, 2, 3} on numbers of gastro-intestinal lymphoid tumors has been most helpful in emphasizing the importance of this tumor and clarifying many of its growth characteristics. However, the distinction between solitary and generalized tumors has not often been made and there has been little discussion of the relative importance and behavior of the different histologic types. Lesions of the stomach have been stressed more than those occurring in the intestine.

Among 3,132 malignant tumors of the gastro-intestinal tract (chiefly surgically removed) studied in our laboratories, there are 28 (0.9 per cent) cases of solitary lymphoid tumors†. We have discarded from our series several other cases originally diagnosed as lymphoid tumor of the gastro-intestinal tract, concerning which there was some doubt as to the classification when they were reviewed.

Pathology—Because of the present incomplete knowledge of the pathology of tumors of lymphatic tissue and the consequent confusion of terms, we have adopted the term lymphoid tumors to indicate the group of primary tumors originating from the cells of lymphatic tissue.

* We have included one case of lymphoma of the stomach in which there were multiple nodules of the stomach, grossly distinct, but probably representing a single tumor.

† We are indebted to the surgical staffs of the Huntington, Pondville, and Deaconess Hospitals for clinical data.

The histopathology of lymphoid tumors of the gastro-intestinal tract does not differ from those of lymph nodes. The absence of uniform terminology impels us to give a brief explanation of our classification.

We recognize four types of lymphoid tumors. Malignant lymphoma, Hodgkin's disease, lymphosarcoma, and reticulum cell sarcoma. All but the last are represented in our series. Malignant lymphoma is composed of quite well-differentiated medium and small lymphocytes, with usually few mitoses. This must be differentiated from the rare benign lymphoma which appears to be a true noninvasive tumor of lymph nodes and may occur as an isolated nodule in the intestine, localized, usually, in the submucosa and presenting a picture quite distinct from hyperplasia.

Hodgkin's disease presents a very variable picture and may be characterized by several or all of the following: Sternberg cells, pleomorphism, eosinophilia, necrosis, and fibrosis. In disease of long duration, fibrosis is sometimes the outstanding feature. Sternberg cells may be so large and numerous as to suggest an undifferentiated carcinoma.

Lymphosarcoma is a rapidly growing tumor, the cells relatively immature, quite uniformly large and pale, with numerous mitotic figures. Many of the cells resemble large lymphocytes and lymphoblasts. Some of them appear to be reticulum cells. Ignorance of the exact nature of these cells has given rise to much controversy. The tendency now is to consider most of these tumors of reticulum cell origin. We believe true reticulum cell sarcoma to be extremely rare, although proliferation of reticulum cells is often present in all forms of lymphoid tumors. Tumors that would be called reticulum cell sarcoma by some pathologists are grouped in our series as lymphosarcoma. Ewing⁴ believes that some lymphosarcomata arise from reticulum cells, others from lymphocytes, and intimates that lymphosarcoma differs in behavior depending upon whether it arises from lymphoid cells or reticulum cells. So far as we know, there are no clinical grounds for distinguishing between lymphosarcoma and reticulum cell sarcoma. We should like to take issue with the concept that reticulum cell sarcoma is more resistant to radiation than other forms of lymphoblastoma. Of two authorities for this statement, one⁵ gives no supportive evidence and the other⁶ presents cases which are at best incomplete.

The 28 tumors presented in this paper are classified as follows: thirteen Hodgkin's disease, ten lymphosarcoma, five malignant lymphoma. Fourteen of the tumors are of the stomach, eight of the large intestine, and six of the small intestine. In 23 of these cases, the tumor was solitary with no evidence of metastasis in any other part, either local or distant, five cases had adjacent lymph node involvement.

The age and sex differences are not significant. The median age at the time of first examination was 53 years, with a range from 20 to 75 years. The ratio of males to females was 9.5—a preponderance of males over females which is present in all forms of lymphoblastoma and of gastro-intestinal

malignancy as well, and probably of no significance. We will consider the tumors of different parts of the gastro-intestinal tract separately.

TABLE I
STATISTICAL SYNOPSIS OF THE SITES OF TUMORS OF THE GASTRO-INTESTINAL TRACT

	Malignant Lesions	Primary, Solitary Lymphoid Tumors	Percent- age	Hodgkin's Disease	Lympho- sarcoma	Malignant Lymphoma
Stomach	569	14	2.5	6	6	2
Small intestine	53	6	11.3	4	1	1
Large intestine	2,510	8	0.3	3	3	2
Totals	3,132	28	0.9	13	10	5

TUMORS OF THE STOMACH

There are 14 cases of lymphoid tumors of the stomach, on 13 of which we have fairly complete data. Most individuals had rather general complaints. Half of the cases presented one or more of the following symptoms: indigestion, anorexia, nausea, and vomiting. Three cases, presenting marked anemia, weight loss and blood in stools of gastric contents when first seen, died two weeks, one year, and three years, respectively, following operation. Total acidity and free HCl were slightly low in four out of six cases. Occult blood was demonstrated in gastric contents in three of six cases, and in one case a tumor, measuring 15 cm., was accompanied by marked anemia and blood in stools, the patient died two weeks after operation.

Roentgenologic examination led to the diagnosis of cancer in three cases, malignancy in four others, and benign ulcer in two cases. In one, the roentgenographic picture was interpreted as compatible with gastritis, lymphoid tumor or carcinoma. A gastroscopic examination (the only one performed upon any of these patients) was unsatisfactory. Celiotomy was performed in each case, and resection of the tumor in ten, two cases were inoperable. A biopsy was taken from each of these two tumors. A total gastrectomy was performed in one case with extensive tumor. Postoperative irradiation was given in three cases.

All of the tumors were large, half of them were over 5 cm., and three of these were over 10 cm., the smallest was 2 cm. in greatest diameter. Six of the tumors involved, primarily, the lesser curvature, and two of them the greater curvature. Although many of the tumors involved a large part of the stomach, the proximal end was less frequently involved than the distal. Two of the tumors extended beyond the pylorus into the duodenum. Three of the tumors showed a slight degree of ulceration. Two tumors had ulcers 2 cm. in diameter, and three tumors had large ulcers 4 cm., or more, in diameter.

In 13 cases, the regional lymph nodes were described as enlarged. In only four of these was there histologic proof of metastasis. In two cases, the tumor had extended beyond the limits of the stomach into adjacent omentum, and in one other case part of the wall had been completely destroyed by necrotic tumor.

Seven of the 14 cases are dead, exitus occurring within a year following treatment in all but one case, in which an interval of three years elapsed between operation and death. Three of these were inoperable. A fourth case died one year after subtotal gastrectomy. The tumor had perforated the

FIG 1



FIG 2

FIG 1 —Stomach—Hodgkin's disease, diffuse type. Male, age 57
Living three years

FIG 2 —Small intestine—malignant lymphoma, diffuse infiltration
Male, age 45. Living six years

stomach wall and extended into the gastrocolic ligament at the time of operation, and was obviously not entirely removed. Death in the fifth case, a year after operation, may also have resulted from extensive tumor since this is the only example we have of multiple nodules of lymphoid tumor in the stomach

However, the serosal coat was smooth and lymph nodes negative at the time of operation. No autopsy was performed. The cause of death in the sixth case, a male 75 years of age, dying six months following operation, is rather obscure, as the tumor, while large, was of mature cell type and low histologic malignancy, with no metastasis at the time of operation. The tumor was supposedly present at death, though this was not confirmed by autopsy. The



FIG. 3.—Colon—Hodgkin's disease, discrete type. Male, age 59.
Died one and one half years after first being seen.

seventh death was a male, 49 years old, who lived three years after excision of a rather extensive Hodgkin's disease without known secondary growths. The status of the tumor at death is not known.

It is worth noting that the tumors in all seven cases were solitary, without secondary distant deposits, and that, although disease was supposedly present at death in five cases, there were only two autopsies, and the cause of death in the other cases is not clear. The two autopsies showed the tumor still localized in the region of the stomach with no secondary deposits.

There are six cases still alive, and five of them without evidence of disease, one, two, three, four and nine years, respectively. One patient is living with disease a year after subtotal gastrectomy. Another patient had a tumor of the lesser curvature and posterior wall (10x7 cm.) resected four years ago, at the age of 72 years. There was no lymph node involvement at that time, but postoperative radiation was given (1,200 r. through two epigastric portals). Two years later, multiple lesions were found in the lungs which suggested tumor. There was also evidence of recurrence in the intestine. In November, 1938, six spray, high voltage roentgen ray treatments, of 30 r. each, were given to the chest and to the left side of the abdomen. The patient is alive four years following excision of the tumor, and two years since the last roentgen ray treatment. There is no definite evidence of disease at present. One patient, having had a subtotal gastrectomy two years ago, is lost.

TUMORS OF THE SMALL INTESTINE

There are six cases of lymphoid tumors of the small intestine, three located in the ileum, one in the jejunum, and two in unspecified locations. The symptoms were of little diagnostic import. All of the tumors were invasive, and the lumen tended to be narrowed rather than dilated. One of the patients with a lobulated tumor, apparently originating at the mesenteric attachment of the ileum, is living without disease six years later. The tumors were large, measuring 5, 5, 7, 9, 15, and 18 cm in greatest diameters. Two of the largest tumors were deeply ulcerated. Three of the tumors had extended slightly into the mesentery. There were no lymph node metastases of any tumors at the time of operation.

Three cases were resected, and are living two, two, and six years after operation, without evidence of disease. Tumors in these cases were diagnosed Hodgkin's disease, lymphosarcoma, and malignant lymphoma, respectively. One untreated case, seen first a few weeks before death, was extremely emaciated at that time and presented a large tumor in the left upper quadrant. Roentgenograms were negative. At autopsy, the tumor mass proved to be Hodgkin's type, infiltrating two adjacent loops of jejunum and forming a single, hollow, honeycombed mass with no secondary deposits in other tissue. One patient died of peritonitis two days after resection of a tumor of the ileum (Hodgkin's disease) infiltrating 7 cm of the length of the wall. One patient with Hodgkin's disease of the ileum is lost.

TUMORS OF THE LARGE INTESTINE

There are eight patients with lymphoid tumor in the colon. There is only one female in the group. Three of the tumors were polypoid, arising in the rectum, one was located at the hepatic flexure, one involved an unspecified portion of intestine and had extended into the mesocolon, three tumors were located in the cecum, two of them large and invading adjacent tissue, and the third lobulated.

The tumors were much smaller than those in the stomach and small intestine, the largest being 8 cm, two others 5 cm and the others smaller.

A history of clinical symptoms was available in only three cases. One patient, a male, 59 years of age, had had symptoms for three months, occasional nausea, rare vomiting, anorexia, and lately anemia, weakness, progressive weight loss (25 lbs), with constipation and recent obstipation. The tumor was firm, lobulated, annular, 5 cm in diameter, with no ulceration. There was no extension into the serosa. Adjacent lymph nodes were involved by tumor. An intussusception of the ileum through the valve had occurred. The patient died two years later. No autopsy was performed but the tumor was said to be present. Another patient, a 23-year-old male, with lymphoid tumor of the cecum, had had mild symptoms for one year, nausea and occasional vomiting, with right lower quadrant pain, and a palpable mass for six months. At operation, at another hospital, a supposedly inoperable tumor of the cecum was found and a colostomy performed. The microscopic diagnosis

SOLITARY LYMPHOID TUMORS

TABLE II

SUMMARY OF MORTALITY STATISTICS OF 28 CASES OF SOLITARY, PRIMARY LYMPHOID TUMORS OF THE GASTRO-INTESTINAL TRACT

Hodgkin's Disease										Lymphosarcoma										Malignant Lymphoma																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																														
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Stomach	No of Cases			Followed			Surgery			No of Cases			1-3			3-5			5+			No of Cases			1-3			3-5			5+			No of Cases			1-3			3-5			5+			Total No of Cases			Total Followed			Total 1-3 Years			Total 3-5 Years			Total 5+ Years			Total Living†																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																					
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* One patient was inoperable, and was irradiated

† One patient died—no therapy

‡ Ten living with no evidence of disease

of a biopsy was "anaplastic carcinoma." A few months later the tumor was excised at Pondville Hospital, and it proved to be a lymphosarcoma. The tumor, 5 cm in greatest diameter, appeared quite superficial, extending only slightly into the muscle. There was shallow ulceration. Enlarged regional lymph nodes, found at operation, were hyperplastic and not invaded by tumor. The patient is now alive and well, without disease five years after operation.

The third patient, on whom we have clinical data, had been treated for the past 11 years for duodenal ulcer. The immediate indication for investigation was the appearance of tarry stools for six months. A small polyp, 1 cm in diameter, was excised from the internal rectal sphincter, followed by roentgenotherapy. The tumor was a typical lymphoid tumor, classified as "inalignant lymphoma." The patient is living, without disease four years later. One other patient with polypoid tumor of the rectum (Hodgkin's disease), 3 cm in diameter, is alive without disease two years after excision. The third case of polypoid tumor of the rectum (lymphosarcoma), 3 cm in diameter, is lost. Another case is lost, that of lymphoid tumor of the hepatic flexure (Hodgkin's disease), measuring 8 cm in diameter. The last case was a large (size not known), ulcerated, annular tumor of the cecum (lymphosarcoma). The patient, a 20-year-old male, died six months after operation, and the autopsy revealed a tumor extending through the retrocecal region into the right kidney and invading the pancreas and peripancreatic nodes.

Aside from two patients with polypoid lymphoid tumors of the rectum, there is only one patient known to be alive, this patient is without disease five years after right colectomy.

Discussion—The foregoing statistics indicate that neither the type of lymphoid tumor nor the location causes any significant variation from the average prognosis. The average survival was 2.5 years. One patient has been living over a year, with disease present. Ten patients are alive for periods of one to nine years postoperatively, with no evidence of disease. Among these there are three five-year cures.

From a review of this group of 28 cases, few conclusions are possible which would help in establishing the clinical diagnosis of lymphoid tumors. But there are a few considerations which suggest that a given tumor may be of lymphoid type. One of the most important is the relatively good condition of a patient presenting a large tumor. Patients with carcinomata as extensive as the majority of the solitary lymphoid tumors, usually present a striking picture of debility. This is particularly true of lymphoid tumors of the stomach. Those in the intestine may cause early, general symptoms related to anemia. In the stomach, the diagnosis must be suspected whenever a large tumor is accompanied by ulcer-like symptoms and vomiting of nonobstructive type. Hematemesis from a tumor in a young person may also be suggestive. In only one of our cases was lymphoid tumor considered in the differential diagnosis, with carcinoma and gastritis as alternatives. Two of our lymphoid tumors of the stomach were thought to be simple ulcers, from

the roentgenograms There are no roentgenologic features diagnostic of lymphoid tumors and, as a rule, roentgenograms are helpful only insofar as they point to a tumor But certain aspects are pertinent In a typical instance, the stomach shows a slightly raised tumor, neither annular nor constricting, with a central, superficial ulcer Large hypertrophic rugae in the stomach, either with or without a filling defect, may suggest the disease The small intestine usually shows an encircling growth which may cause either enlargement or diminution of the lumen in the affected part Special technics are useful in assuring a more complete study of small intestine than is ordinarily attainable⁷

Gross Pathology—The gross appearance, on the other hand, is often quite well-defined Lymphoid tumors, in whatever part of the body they may occur, grow along lines of least resistance, to an extent not seen in other malignant growths As a result, tissues are separated along cleavage planes, thus accentuating different structures, such as mucosa, submucosa, and muscularis, and producing fairly uniform, diffuse enlargement of the part invaded It is only later, when the growth is more exuberant, and normal barriers are broken down by pressure of the proliferating tumor cells, that structures are obliterated and necrosis occurs There are two main types of growth seen in lymphoid tumors (1) Diffuse growth involving a large part of an organ, causing fairly uniform, diffuse thickening, sometimes with discrete tumors here and there, with or without ulceration, and (2) a large solitary tumor, with usually deep ulceration or rather cavitation Rarely, polypoid forms of the tumor are seen

The serosa is not invaded or distorted by lymphoid tumor, except in rare cases when the tumor is very large An extensive tumor, which does not greatly distort the organ or involve the serosa, is very likely to be of lymphoid nature

Lymphoid tumors, usually, are succulent and more resilient than most carcinomata, although Hodgkin's disease may present a very firm, fibrous structure They are rarely recognized when they are small, and when first observed are usually much larger than carcinomata

Other lesions having gross features in common with lymphoid tumors are Diffuse carcinoma simplex, leiomyoma and leiomyosarcoma, and a diffuse inflammatory change such as cicatrizing enteritis and syphilis of the stomach Diffuse carcinoma simplex, fairly commonly seen in the stomach but rare in other parts of the intestinal tract, may cause a uniform thickening of the wall, separating without distorting the structural units in a manner similar to that of lymphoid tumors with the difference that this type of carcinoma produces a rigid, contracted organ, and is frequently mucus-secreting

Most inflammatory conditions are easily distinguished from lymphoid tumors, but cicatrizing enteritis (regional ileitis) may cause a diffuse, uniform thickening without loss of structure Diffuse gastritis, especially of syphilitic origin, may, similarly, be confusing to differentiate

The large, globular, lymphoid tumors may resemble leiomyoma or leiomyosarcoma. The benign and malignant forms of smooth muscle tumors are rarely seen in the gastro-intestinal tract, but are somewhat more common in the stomach than elsewhere. They usually present as a discrete, rounded, resilient tumor, either intrinsic in the wall or pedunculated toward the mucous or serous surface. Even when the histologic structure is that of a fairly malignant tumor, the growth tends to be delimited rather than invasive. Necrosis and ulceration are the usual signs of malignancy and rapid growth. The lymphoid tumors, though expansile, do not often become pedunculated.

It is important to determine whether or not the tumor is part of a generalized disease. This is a more important problem in the small bowel, where secondary, lymphoid tumors are more commonly found. The most helpful consideration is the infrequency of secondary tumors in the small bowel without large metastases in either the mesenteric or retroperitoneal lymph nodes. Secondary lymphoid tumors are less common in the stomach and large bowel, and practically never reach the size of the usual primary, lymphoid tumor.

Treatment—All of our cases were treated, primarily, by surgical excision, all but three being removed at operation, one of these was inoperable, the tumor was biopsied and irradiated. Two patients died without therapy, but biopsy was taken in one of these cases. Two cases of lymphoid tumors of the stomach received postoperative roentgenotherapy, and are living and well, without disease three and four years after treatment. Both were Hodgkin's type. Because of the uncertainty in the diagnosis of lymphoid tumors, either with or without biopsy, excision is the treatment to be preferred. Postoperative irradiation may be definitely beneficial for those tumors which cannot be completely removed. In the literature, there are reports of at least nine four-year cures by irradiation alone^{2, 8}. This suggests that this therapy may assume greater importance in the future,^{2, 9} in spite of certain dangers in radiation of tumors involving a hollow viscus.

Discussion—Solitary, lymphoid tumors of the gastro-intestinal tract are of not infrequent occurrence and should be considered in differential diagnosis. It may be useful to compare these tumors with solitary, lymphoid tumors arising primarily in other regions. Lymphoid tumors of the skin, without evidence of lymph node or organ involvement, have long been recognized and often classified under the broad descriptive term of "mycosis fungoides"¹⁰. These tumors in the skin may be the first manifestation and sole evidence of disease for many years. The majority of the patients that come to autopsy have similar tumors involving either lymph nodes or organs.

Lymphoid tumors of the bone of the reticulum cell type have been described with increasing frequency during the past ten years¹¹. In cases reported by Parker and Jackson,¹² and in cases reported by Simmons,¹³ secondary foci of tumor have developed in only a few cases after several years of observation.

Whether the tumor is in the skin, bone, or gastro-intestinal tract, the dis-

inction must be made between the tumors which are primary and remain solitary for some time, and those in which the first evidence of disease happens to be a local process in these tissues, soon to be followed by generalized disease

In studies of a small series of cases of solitary, lymphoid tumors, in skin, bone, or gastro-intestinal tract, one has the impression that these tumors have a relatively benign course in contrast to other forms of malignancy in the same locations, and as against generalized lymphoid tumors. Operative removal frequently results in cures for five to 15 years. But there are, as yet, too few reported cases for any volume of statistics to have accumulated from which one may draw conclusions. The average duration of life of our 28 primary lymphoblastomata of the gastro-intestinal tract is 2.5 years, comparable to three years, reported by Madding and Walters³. The life expectancy for generalized lymphoid tumors is two years, as reported by Nathanson¹¹.

SUMMARY AND CONCLUSIONS

In a series of 3,132 malignant lesions of the gastro-intestinal tract there are 28 cases of primary, solitary lymphoid tumors, an incidence of 0.9 per cent.

The characteristics of these tumors have been considered from the point of view of clinical symptoms, treatment, and outcome, and the gross and microscopic pathology.

These tumors remain solitary for many years, and may reach a large size before causing disturbing symptoms.

Metastasis to regional lymph nodes and extension into adjacent tissue occur late in the disease, if at all.

The behavior of primary, solitary lymphoid tumors in the gastro-intestinal tract is not unlike that of similar tumors in bone and skin.

In this series, the prognosis for the solitary form is but little better than for generalized lymphoid tumors, but in many cases long survival periods and possibly complete cures have been obtained by adequate treatment.

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RUPTURE OF THE COLON BY COMPRESSED AIR

REPORT OF THREE CASES

ROSWELL K BROWN, M D ,
BUFFALO, N Y

AND

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AUBURN, N Y

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COMPRESSED AIR came into rather general use in industry at about the beginning of the twentieth century. In 1904, Stone¹ reported a fatal case of rupture of the bowel caused by compressed air introduced per rectum from a machine which was pumped by hand. In 1908, Petien² wrote about a case of fatal rupture of the esophagus from accidental oral insufflation. In 1911, Andrews³ reported a case of pneumatic rupture of the sigmoid colon which recovered following resection of the injured loop. He also discussed the subject quite completely and recorded 15 other cases collected by correspondence and from law reports. Later in the same year, Lenormant⁴ reviewed the previous papers and discussed the subject editorially in the *Presse Medicale*, of Paris. The following year, Cotton⁵ reported the recovery of a case of perforation of the ascending colon—he established a temporary colostomy at the site of the perforation and repaired several rents in the serous and muscular coats of other portions of the colon. In 1914, Bendixen and Blything⁶ reported another recovery—a case of pneumatic rupture of the transverse colon, and gave brief notes on seven collected cases which were fatal. Buchbinder⁷ reported a fatal case in 1921.

There have been a number of more recent publications on this subject. Table I gives a brief summary of cases of complete rupture of the bowel from compressed air that we have found in a rather thorough search of the literature.* Hays¹³ was apparently the first American author who was aware of Stone's original contribution. Burt¹⁶ found that under experimental conditions the human colon bursts with only about 4 lbs pressure, and that the serous and muscular coats tear first at about 3½ lbs pressure. Table II summarizes cases of incomplete rupture of the bowel. These two tables, and our bibliography, are arranged according to dates of publication. Our three cases illustrate various degrees of severity of bowel injury from compressed air.

CASE REPORTS

Case 1—Dr James H Lewis. Complete Rupture of Transverse Colon with Marked Abdominal Distention. H Z, white, male, age 21, was admitted to the Moses Taylor

* Data on two cases of Fauquez (Burt¹⁶), one of Houzel (Burt¹⁶), and one of Semerikov²⁰ are not included.

TABLE I

PNEUMATIC BOWEL PERFORATION

No	Author	Year	Age	Pounds Press- ure	Opera- tion	Treatment		Site of Perforation	Result
						Time After Injury			
1	Stone	1904	17	20	Yes	(trochar)		Sigmoid	Died
2	Andrews	1910		60	Yes	5 hrs		Sigmoid	Recovered
3	(1) Fletcher	1907	36	70	Yes	4½ hrs		Sigmoid	Recovered
4	(2) Tilney	1907	21	—	No			—	Died, third day
5	(3) (Curnie)	1906	—	40— 100	Yes	?		—	Died
6	(4) (Ballard)	1908	—	—	No			—	Died
7	(5) Boughton	1910	39	—	Yes			Sigmoid (3 places)	Recovered
8	(6) Stevens	1910	20	—	Yes	9 hrs		Splenic flexure	Died
9	(7) Sherman	—	—	—	No			—	Died (autopsy)
10	(8) (Banquet)	—	25	—	No			Rectum (2 places)	Died (autopsy)
11	(9) (Kaseberg)	1908	22	—	No			Rectum	Died (autopsy)
12	(10) (Borgan)	1906	25	—	No			Rectum	Died (autopsy)
13	(11) (Jaworski)	1905	47	—	Yes			Sigmoid	Died (autopsy)
14	(13) Burry	1907	20	125	Yes			Colon (3 places)	Died (autopsy)
15	(15) Godfrey	1908	19	80	No			Upper end sigmoid	Died (autopsy)
16	Cotton	1912	—	—	Yes	3 hrs		Ascending colon	Recovered
17	Bendixen & Blything	1912	20	100— 125	Yes	2 hrs		Transverse colon	Recovered
18	(1) (Orth)	1908	—	—	Yes			—	Died 3 hrs
19	(3) (Dagenais)	1906	15	—	Yes	4 days		Sigmoid	Died (autopsy)
20	(5) (Denney)	—	—	—	No			—	Died
21	(6) Groman	—	15	—	Yes	After trochar		Near cecum	Died
22	(7) Meecray	1913	17	10	No			Colon (8 places)	Died (autopsy)
23	Buchbinder	1920	—	85	Yes			Sigmoid (gangrene)	Died (autopsy)
24	Jean (1)	—	—	—	Yes	4 hrs		Rectosigmoid junction	Recovered
25	(2)	—	—	—	Yes	2½ hrs		Sigmoid	Recovered
26	Hailes	—	—	—	Yes	19 hrs		Colon	Died
27	Sparkman	1922	—	—	Yes	3 hrs		Sigmoid	Recovered
28	Block & Weissman	1925	45	125	Yes	5½ hrs		Sigmoid	Recovered
29	Hays	1923	30	95	Yes	1 hr 50 min		Rectum	Recovered
30	Patterson	1930	—	—	Yes			Hepatic flexure	Recovered
31	Burt (1)	—	49	2	Yes			Iliac (old colitis)	Died
32	(a) Shoudy	1927	—	—	Yes			Many	Recovered
33	(b) Shoudy	1916	—	—	No			—	Died
34	(c) Shoudy	1927	—	—	Yes			—	Recovered
35	(2) Moorehead	1928	37	—	Yes	25 hrs		Sigmoid (3 places)	Recovered
36	Ide	1930	—	—	Yes	3 hrs		Sigmoid	?
37	(1) L F	—	12	—	Yes			Rectum sigmoid and descending colon	Died
38	(2)	—	—	—	Yes			Lower end of sigmoid	Died
39	(3)	—	—	—	No			—	Died
40	(4) C R	1920	—	—	No			—	Died
41	(5)	1918	16	—	?			—	Died
42	(6) Nilsson	1926	—	—	No			—	Died
43	(7)	1914	21	—	Yes			—	Died
44	(8)	—	—	—	No			—	Died
45	(10) Wainwright	—	—	90	Yes	6 hrs		Loud explosion	Recovered
46	(11)	—	—	—	Yes			Sigmoid	Recovered
47	(12)	—	—	—	Yes			—	Died, 5 hrs
48	(13)	—	—	—	No			—	Died, 24 hrs
49	(14)	—	—	—	No			—	Died
50	(15)	1936	—	—	No			—	Died
51	(16) Mr P	—	—	—	No			—	Died
52	(17) A L	—	—	—	?			Colon	Died

PNEUMATIC RUPTURE OF BOWEL

TABLE I (Continued)

No	Author	Year	Age	Treatment		Site of Perforation	Result
				Pounds Press-ure	Opera-tion		
53	(18)	1915	—	—	No	Rectum	Died 3 hrs
54	(19) J H	1915	—	—	?	—	Died
55	(20)	1920	—	—	?	Colon	Died, 8 days
56	(21)	1936	—	90	Yes	—	Died during operation
57	(23) Cereal	—	—	—	?	—	Died
58	(24)	—	—	—	?	Sigmoid	Died
59	(25)	—	—	—	?	—	Died
60	Ritchie	—	—	—	Yes	6 hrs Sigmoid	Recovered

TABLE II

PNEUMATIC BOWEL INJURY WITHOUT PERFORATION

No	Author and Case Mark	Date	Age	Lbs Air Press-ure	Treat-ment	Pathology	Result
1	Andrews XII Kahlke	1906	20	—	Operation, 18 hrs	Colon ruptured entire length except for 1 or 2 narrow bands Mucosa was not perforated	Died
2	XIV Burry	1908	—	—	None	Insufflation with live steam	Recovered
3	Bendixen & Blything (Orth)	1913	16	85	None	Returned to work shortly	Recovered
4	(Kay)	1905	—	—	None	Recovery rapid and complete	Recovered
5	Schwartz	1922	—	20-70	Operation, 6 hrs	No perforation found but serous and muscular coats of large intestine were lacerated	Recovered
6	Morris	1923	—	60-65	Operation	Mucosa bulged through 7-inch tears on each side of cecum Sigmoid had a number of small tears, but mucosa not ruptured	Recovered
7	Ide IX	1929	—	—	None	Not serious, returned to work in 10 days	Recovered
8	XXII	—	—	—	None	Injuries minor No disability	Recovered
9	Neese	1936	42	75	Operation	Multiple areas of herniation of mucosa of descending colon and sigmoid—due to tearing of serous and muscular coats No perforations	Recovered

Hospital, April 1, 1915 He had collapsed immediately after air was released from a nozzle which was held against the seat of his trousers At the time of admission he was in profound shock Temperature, by mouth, 96° F, pulse 92, respirations 26 The abdomen was markedly distended, liver dullness to percussion was absent The lower extremities were blue and cold There was a protrusion at the anus, and prostatic secretion was noticed at the urinary meatus A rectal tube was inserted but no air escaped Vomitus was fecal

Operation—About two hours after the injury Under general ether anesthesia, a midline incision above and below the umbilicus was made The skin and underlying tissues retracted widely When the peritoneum was opened there was a sudden deflation The pelvis contained a brownish-red fluid There were several tears through the serous and muscular coats of the transverse colon and in its midportion there was an opening through the mucous layer about one inch long Both the ascending and descending colon had been loosened from the parietes in places, at the iliocecal junction there was an ecchymosis three inches in diameter The small intestines contained air and the gall-bladder was distended with air, being three and one-half inches long and one and one-half

inches in diameter. The perforation was sutured, the peritoneal cavity was sponged grossly clean, drains were inserted, and the wound was closed.

The postoperative course was stormy. A fecal fistula developed, which closed spontaneously. The patient left the hospital in good health 90 days after the accident.

Case 2—Dr. James H. Lewis. Incomplete Ruptures of Rectum and Sigmoid Colon. J. B., white, male, age 40, was admitted to the Moses Taylor Hospital, August 6, 1916, complaining of abdominal pain and vomiting, which occurred immediately after his fellow workmen released the compressed air against his anus. Temperature 96.8° F, pulse 74, respirations 20. He seemed to be in great pain and was dazed. There was slight rigidity in both lower quadrants of the abdomen, but there was no bulging or distention.

Operation—Six hours after injury. Under general ether anesthesia, an incision was made in the midline below the umbilicus. There was no noticeable escape of air when the peritoneum was opened. There were five tears in the serous and muscular coats of the sigmoid colon, and one of the rectum, but no perforation in the mucosa was discovered. These tears were sutured and the abdomen was closed. A rectal tube was inserted. The patient made an uneventful recovery and was discharged from the hospital 30 days after the injury.

Case 3—Drs. Brown and Dwinelle. Complete Rupture of Sigmoid Colon, without Abdominal Distention. W. R., white, male, age 24, was admitted to the Moses Taylor Hospital, July 29, 1939. The patient had a tear along the seam of his trousers on the medial aspect of his thigh, into which a fellow workman, jokingly, had directed the compressed air jet. He felt some pain in the upper part of the abdomen and had to sit down because of weakness. In a few minutes he felt better, changed his clothes and walked to the dispensary. Temperature 99° F, pulse 88, respirations 20, blood pressure 120/84. At this time he had practically no pain. There was no distention of the abdomen, there was no rigidity, and only slight tenderness just above the symphysis pubis. There was no area of dulness to percussion in the region of the liver. A roentgenogram of the abdomen in the erect position showed air between the diaphragm and the liver (Fig. 1).

Operation—Four hours after the injury. Under general ether anesthesia, a low left rectus incision was made. The peritoneum was opened beneath sterile saline solution, air bubbled out as soon as the peritoneum was incised. There was a little blood mixed with fecal material in the pelvis. An irregular stellate rupture about two inches long in the lower part of the sigmoid flexure was sutured with silk with considerable difficulty. A rectal tube was guided up past the site of injury, cigarette drains were placed on either side of the injured bowel, and the abdomen was closed in layers. A fecal fistula developed which closed spontaneously 24 days after the accident. The patient left the hospital in good health on the 58th day.

Pathogenesis—This accident is not uncommon, because the public is not aware of the fact that a compressed air jet is a lethal weapon. All the victims were males, between the ages of 12 and 49. Many cases are due to pranks, but not all of them. Workmen should never dust off their clothes with compressed air.

The jets that are used in industry are usually said to have a pressure of from 50 to 100 lbs. or more. The nozzles are pipes one-quarter to one inch in diameter, sometimes the rubber hose is used without a nozzle. Usually one thinks of these jets in terms of experience with visible streams of water from a nozzle, but the gaseous jet differs in that it is elastic and expands in all directions, adapting itself to surroundings, bending and twisting and causing eddy currents.

Such an air jet enters the anus more readily than the examining finger or a proctoscope, as it passes through clothing and enters the bowel even when not accurately directed at the anus, as in Case 3. It has been suggested³ that the thighs, buttocks and perineum form a funnel which delivers the stream of air to the anus. Gases under pressure pass through small apertures very rapidly. Compressed air has been known to enter a hangnail accidentally and produce signs suggestive of gas gangrene of the hand and forearm.

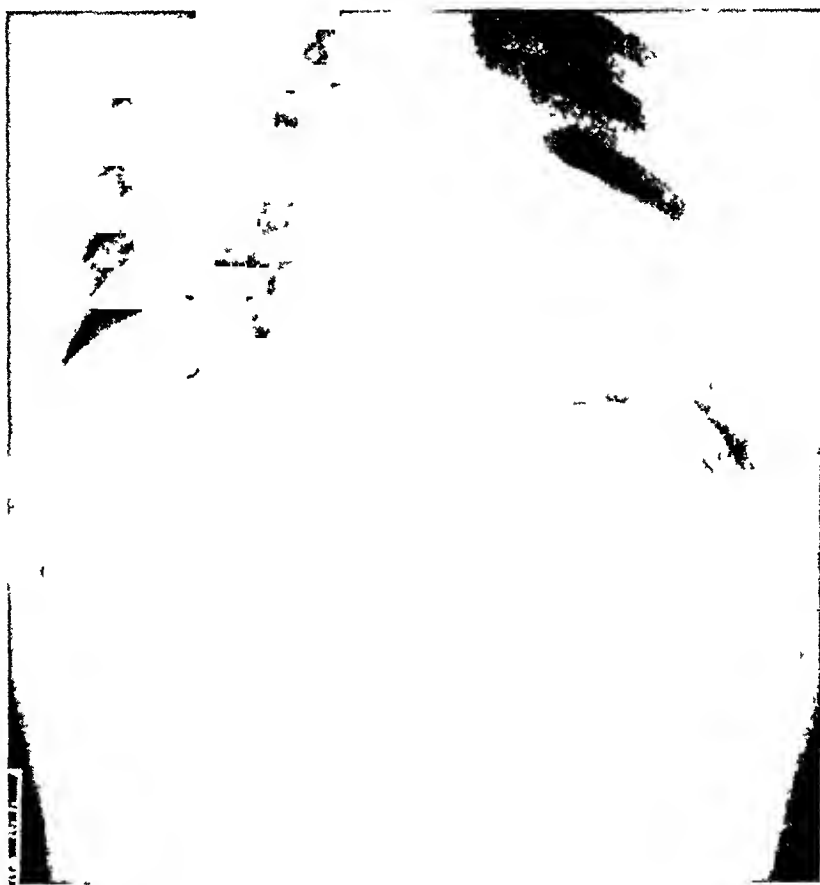


FIG. 1.—Case 3. Preoperative roentgenogram, sitting up. Shows gas beneath the diaphragm.

Rupture of the intestine perhaps depends more upon the suddenness of the pressure than upon its amount, for the bowel will expand enormously if given time to relax. Duval (quoted by Burt¹⁶) observed great dilatation of the colon in a deranged patient who inflated himself by means of a hand bicycle pump. Operation was performed in error, with a diagnosis of megacolon, and no abnormality was found.

Apparently the muscularis mucosae adapts itself more readily to sudden changes in tension than the outer muscular coats of the bowel. Rents in the muscle, usually along one of the longitudinal bands, with the underlying mucosa intact, have been observed in many cases. Case 2, and at least some of those listed in Table II, illustrate the occurrence of these incomplete lacerations without any associated complete perforation. The inner mucosal tube balloons out through the split outer muscular tube, like the "blow-out" of a pneumatic tire. The bursting defect in the inner tube is usually smaller than

the rent in the outer tube, it may retract beneath the edge of the outer tear. When there are multiple lacerations, complete rupture through all the layers is usually found in only a few, perhaps in only one of them. The most common lesion is a complete perforation at the angulation where the sigmoid colon joins the rectum, as in Case 3.

Figure 2 shows the approximate distribution of perforations in 32 cases. Autopsy records of some of the cases in Table I indicate that the injury destroyed the blood supply of segments of the colon (Buchbinder⁷), but this seems to be rare. Tearing of the ascending and descending colon from parietal attachments, as in Case 1, has been observed in a number of cases. The entire intestinal canal may be filled with air. It is difficult to understand how the air got into the gallbladder in Case 1. Subcutaneous emphysema of the trunk occurs when the distention is great.

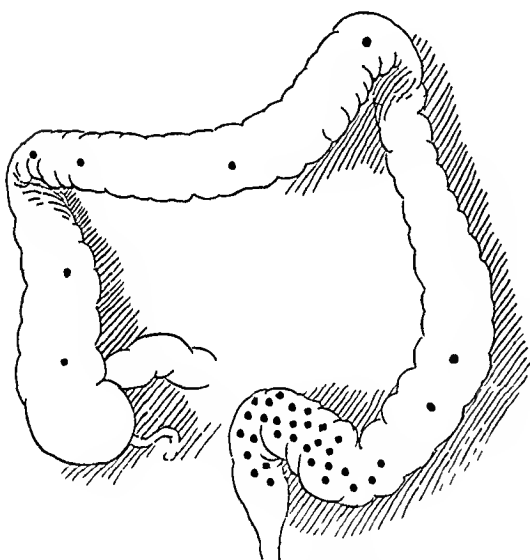


FIG. 2—Schematic drawing showing the approximate location of 38 perforations in 32 cases. Two cases each, had three perforations in the sigmoid colon. One case had two perforations in the sigmoid colon. Twenty-nine cases had single perforations.

Mecray's case (Bendixen and Blything⁶), in which "the colon was ruptured in eight places" and others not definitely described as to location are not included in the drawing.

Diagnosis—The history in these cases has often been obscured by language difficulties, and by attempts to conceal the facts. There should be no difficulty in diagnosis from the history alone, when properly elicited. Abdominal pain is immediate, perhaps most severe in the upper part of the abdomen, radiating to the shoulders. The patient is usually prostrated. In the more severe cases, there is enormous ballooning of the abdomen, with cyanosis resulting from embarrassment of respiration and circulation. Subcutaneous emphysema of the trunk may be present. The uniformity of the tympany over the entire abdomen has been considered diagnostic.

When the distention is not great, the pain in the upper part of the abdomen may disappear, leaving the patient quite comfortable until local pain in the region of the perforation develops, as in Case 3. In this case, obliteration of the liver dulness was the only positive physical sign. Roentgenograms taken with the patient erect show the gas between the liver and diaphragm (Fig. 1).

Treatment—When distention is great, immediate paracentesis should be performed. The general condition may improve remarkably after simple relief of intra-abdominal pressure, even moribund patients may rally sufficiently to warrant celiotomy. To illustrate the tension that may be present we will quote Wainwright (Ide¹⁷): "When the peritoneum was opened there was a loud escape of gas under high pressure, almost as loud as the report of a small automobile tire." Buchbinder's⁷ description is also of interest in

this detail "The transversalis fascia was not incised but sharp-nosed forceps were pushed through in order to control the escape of air. The fascia immediately tore like wet paper under great tension, the air rushed out with a report, and the abdominal wall dropped in. The sudden escape of air nearly proved fatal, but after a few moments the patient rallied, and his general condition seemed much improved."

Rectal tubes are of no avail. Enemata are of course very harmful. Ritchie's¹⁸ case was given a soapsuds enema and then a turpentine enema at home before a doctor was called. The fluid was removed from the peritoneal cavity, the rent in the sigmoid was repaired—and the man recovered.

Operation should be performed as soon as possible. The incision should be large enough for exposure of all of the colon. The defects in the bowel should be closed as quickly as possible. Resection is of course necessary when the blood supply of the bowel has been destroyed by the injury. Usually, simple suture of the rent is sufficient, but it may be difficult because of the irregular shape of the bursting laceration, and because the tear in the mucosal layer does not correspond accurately to that of the muscular layers. Drainage is usually advisable, not only because of the contamination, but also because of doubt as to the adequacy of the closure of the bowel. Colostomy and enterostomy have been performed. If the perforation is at or near the sigmoid flexure, it is better to have a long soft rectal tube inserted while the abdomen is still open, and guide it past the site of injury. The postoperative care is that of any other potential peritonitis case.

Prognosis—Many of the cases listed in the literature are of little value for statistics because insufficient information is given. Table III summarizes the results of treatment. Recovery is usual when only the serous and muscular coats are torn. However, most of the cases had one or more complete perforations, in this larger group the prognosis is grave unless an adequate operation is performed within a few hours.

TABLE III
RUPTURE OF COLON FROM COMPRESSED AIR

	Result Unknown	Recov- ered	Died	Mortality Percentage
<i>Incomplete Rupture</i>				
(Operative cases only)				
Our case #2 and 4 cases from the literature		4	1	20%
<i>Complete Perforation</i>				
Our cases #1 and #3 and 60 cases from the literature	1	19	42	69%
Treatment unknown			7	
Without operation		0	21	100%
With operation	1	19	14	42%

CONCLUSIONS

Pneumatic rupture of the colon is produced by a jet of compressed air, which readily passes through clothing and enters the anus. Perforation

occurs at the rectosigmoid angle or, less frequently, at some other flexure of the colon. Rarely, only the serous and muscular coats of the bowel are torn.

The diagnosis may be made on the basis of the history alone, or by the physical signs alone. Absence of liver dulness may be the only important early physical finding. Roentgenologic examination in the erect position, in order to demonstrate air between liver and diaphragm, is a valuable aid in doubtful cases.

When distention is great and respiration is embarrassed, paracentesis should be performed immediately. Early celiotomy with appropriate repair offers good hope of recovery.

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CONGENITAL MALFORMATIONS OF THE APPENDIX— A FAMILIAL DISEASE

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THE FREQUENT OCCURRENCE of appendicitis in members of the same family is known, and has been remarked by numerous authors^{1, 2, 3, 4, 5} Probably every physician knows, at first hand, of one or more families in which plural appendicectomies have been performed

Baker,⁶ and also Miss M L Nutt, submit several pedigree charts of families who have been subjected to many appendicectomies Discussing this matter editorially, the Journal of Heredity states "Genetic differences in resistance to bacterial infection, a peculiar configuration of the appendix, or other factors about which we at present know nothing, probably constitute a predisposition toward inflammation of the appendix The result, when expressed in a pedigree chart, resembles what we get in the inheritance of a definite morphologic or physiologic difference, but the chain of events leading up to the 'expression' of the 'character' has at least one more link of crucial importance—an environmental trigger-stimulus of some kind"

If congenital anomalies of the appendix are truly a cause of symptoms and offer a predisposition to acute inflammation of the organ, this familial incidence is logical Individual peculiarities of visceral organs ought to be as heritable as peculiarities of feature or complexion, or even of blood groupings, which have been shown by von Dungern and Hirschfeld⁷ to be inherited

Nicholson⁸ has shown convincingly that mechanical deformities of the appendix are responsible for much ill health, poor nutrition and poor development in children He also claims that many cases of appendicitis in later life can be traced back to childhood or infancy if a careful history is taken The inference is that there is often a congenital fault In my own experience, also, it had been common to find that the acutely inflamed appendix has been previously crippled by congenital bands or kinks, which may partially obstruct the lumen

It seems of interest, therefore, to review the history of a family consisting of 22 individuals, representing one man and his descendants to the third generation, in whom appendicectomy has been performed in 16 instances In every individual who has come to operation, the same deformity of the appendix has been found, and it seems likely that this deformity has been at least a predisposing cause of the disease

The family studied includes Nô 1, his six children and fifteen grandchildren Nô 1, four of the six children, and eleven of the fifteen grandchildren have been operated upon

Individuals are distinguished in this study by their initials, the conventional sex symbol, and a numeral to distinguish whether they belong to the first, second or third generation, these symbols are used in the attached chart

N ♂ 1, as far as known, had a healthy childhood and youth. No particular illnesses are remembered, on the contrary, he was strong and robust. All his immediate family had lived to a ripe old age, several surpassing 90 years. His sister, his brother, and his brother's four children have likewise had no appendiceal troubles, neither has there been any such in his wife or her family. The congenital mechanical fault that is found in so many of N ♂ 1's immediate descendants, and apparently inherited, seems to have been present in N ♂ 1 himself.

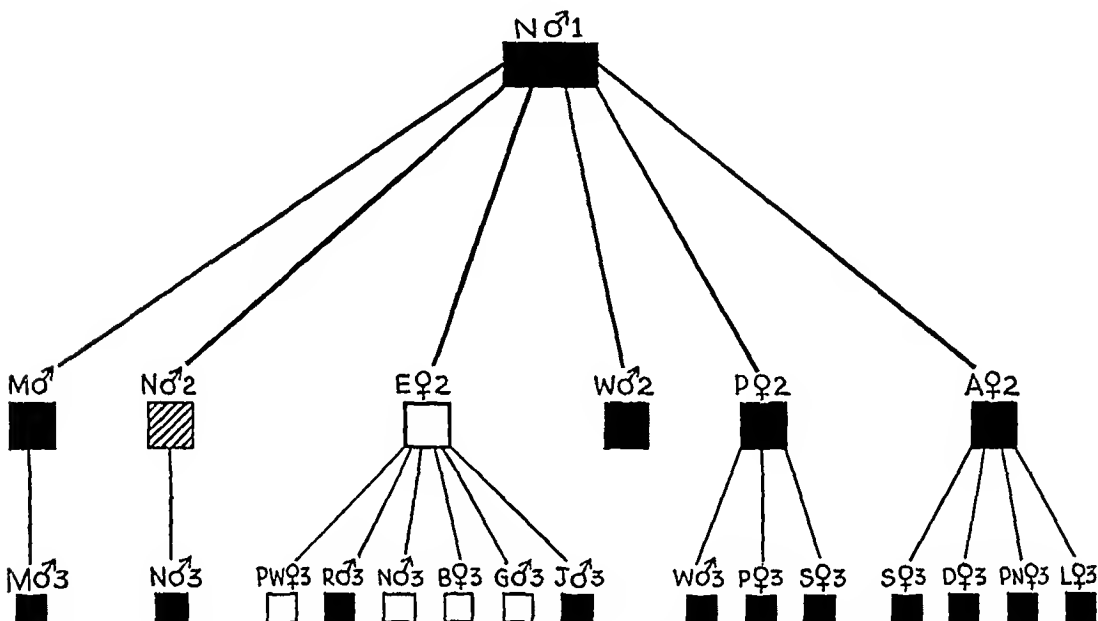


CHART 1—The family tree of N ♂ 1, showing frequency of occurrence of appendicitis in three generations
Key Black—Operated for appendicitis White—No symptoms of appendicitis, never operated upon Shaded—Symptoms of appendicitis, out no operation

This man, a physician, began around the age of 35 to have mild attacks that he diagnosed himself as appendicitis. But, in 1906, appendicectomy was not usually undertaken lightly, so for some years nothing was done. Finally, when he was about age 45, he was operated upon. His appendix was sharply kinked at the base by a band of fibrous tissue, which bound it to the outer side of the cecum—this is the deformity that has been found in every one of his children and grandchildren who have been operated upon. The operation was followed by complete relief of symptoms and freedom from the attacks of abdominal pain and vomiting, until his accidental death a few years later.

Though N ♂ 1 was the oldest of the family, he was not the first to require operation. Already, some years earlier, his fourth child, W ♂ 2, had been hurried to the hospital, and operated upon for acute appendicitis. The records of this illness were very poorly kept, but the boy ran a high temperature for ten days, and was in the hospital three weeks, leaving for home by ambulance. He finally made a perfect recovery.

No more surgery was necessary in the family for ten years or so. During this time N ♂ 2 often confided to his brother, a medical student, that he had a good deal of indigestion, with pain in his abdomen, from time to time, when a point of tenderness could usually be found at McBurney's point. However, the medical student rather feared ridicule if he "stuck his neck out too far," and dared not make the diagnosis of subacute appendicitis, which now seems obvious. Nothing was done. He was admitted into the Air Service in the first World War, serving under the command of Major Fiorello La Guardia, and was killed at the front, with his appendix still *in situ naturalis*.

After the war, the next beneficiary of surgery was M ♂ 2, who, a physician like his father, also made his own diagnosis. This was an acute attack of appendicitis, and had not been preceded by any prodromal symptoms. However, the appendix was acutely inflamed, and there was a similar congenital band and kink such as had previously been found in both his father and brother.

The two sisters P ♀ 2 and A ♀ 2 were next. P ♀ 2 was emaciated, constantly suffered with indigestion, and had McBurney's point tenderness. She was operated upon, and a kinked, deformed appendix was removed, which was not acutely inflamed, but was found in the usual familial position. A ♀ 2 was more robust, but had had many sharp attacks of so-called "colic." From her was removed an acutely inflamed appendix. Both these women have been entirely free of indigestion and colic ever since.

E ♀ 2 has never had any troubles with her own appendix, and only two of her six children have been operated upon as yet. The two boys R ♂ 3 and J ♂ 3 both had acute attacks of appendicitis, and showed the familial deformity seen in all the other cases.

M ♂ 3 was the son and grandson of physicians, so when he began to have indigestion and abdominal pains at the age of eight, no time was lost waiting for a second attack. His appendix promptly came out. It was not acutely diseased, but was deformed.

N ♂ 3 was the only child of a widow, who was not thoroughly convinced that promiscuous appendectomy was a good thing. So he continued to be allowed to suffer from indigestion and abdominal pains till the age of 19. At this time, his appendix gave real trouble, for at operation, about eight hours after the onset of an attack, it was found to be already ruptured. He made a good recovery, and has since been entirely free from discomfort.

The next three grandchildren consist of the son and two daughters of P ♀ 2. Their father and mother have both been appendicectomized. These three children all had mild or severe, acute attacks in early childhood, P ♀ 3, the oldest daughter, drained for several weeks. All had the usual deformity and constriction of the lumen of the appendix, and all have been perfectly well since their operations.

The four daughters of A ♀ 2 have also all been operated upon, with the same operative findings, and the same improvement in health as in the patients noted. Three had acute attacks, one, S ♀ 3 had a chronic condition, with so much anorexia, pylorospasm, and vomiting, that she nearly died of starvation. She was operated upon in 1927, at the age of four, when it was not realized that appendiceal deformities could cause such a serious situation. Her operation was undertaken with a great deal of hesitation by all concerned. The child's almost instant recovery, with gain in weight and strength, was one of the most dramatic things I have ever seen.

Most of the patients mentioned have, by now, reached adult life, though two are still children. All are now normal, healthy individuals, entirely free of any digestive or abdominal disturbances.

It is astonishing, in reading the histories of these cases, to note the close familial resemblance of all these appendices. Though the operations were performed in various hospitals, and the findings recorded by various interns between 1909 and 1938, in every case the record refers to a band of fibrous tissue at the base of the appendix, with more or less adhesion of the organ to the outer surface of the cecum, exactly as in the case of N ♂ 1, the founder of the family.

This family history emphasizes the remarks made as long ago as 1886 by Reginald Fitz,⁹ who stated that "In considering the symptoms of appendicitis, it is to be noted that attacks of inflammation frequently occur without giving rise to any characteristic symptoms, and often without suggestion of any distinct malady. The severity (of the lesions found at autopsy) suggests the

probability that apparently slight disturbances of digestion were overlooked. The diarrhea, constipation, or abdominal pain, especially when occasionally recurrent, were regarded as characteristic of a feeble digestion. There can be little doubt that a diagnosis of bilious attack, colic, gastritis, enteritis, gravel and the like, may not infrequently conceal the existence of an inflamed appendix." Most of these diagnoses have been made in the histories of the second generation of this family. Truly it is said—"There is no new thing under the sun."

SUMMARY AND CONCLUSIONS

This is the history of a family consisting of 22 members—being one man, his six children and fifteen grandchildren, in whom appendicectomy has been performed in 16 instances.

Most of the operations were performed during early childhood. In the adults, most of the symptoms mentioned by Nicholson can be traced back to childhood in nearly all of the cases.

The strikingly good results which, as he shows, follow removal of the mechanically crippled appendix, are borne out in this family.

It is believed that these crippling peritoneal bands may be inherited.

Most of the specimens removed were considered merely routine appendices, and were not particularly examined by the several pathologists. It is believed that the earliest symptoms are due to deranged intestinal function only, of a reflex nature, such as pylorospasm or spastic colon, without organic changes in the appendiceal wall. This was certainly true of S♀ 3, but this series throws little light on this question, which I hope to consider at another time.

The presence of congenital malformations alone is not sufficient to precipitate an attack of acute appendicitis, though they are a predisposing cause. To produce the acute attack, the presence of some other etiologic factor is necessary.

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OBSTRUCTIVE JAUNDICE DUE TO CARCINOMA OF THE PANCREAS THE CHOICE OF OPERATIVE PROCEDURE

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DESPITE recent renewal of interest in the problem of biliary tract obstruction due to carcinoma of the head of the pancreas, treatment of this condition remains as yet almost entirely palliative in nature.

Whipple, and his associates^{15, 18, 19} have made encouraging progress with their operation for neoplasm arising from the ampulla of Vater. However, the multiple-stage procedure which they advocate has been marked, even with them, by a rather high mortality rate. As far as published reports show, they have apparently had two successful resections for carcinoma of the ampullary region.

Clinical instances of radical resection of the head of the pancreas for carcinoma, attendant with any degree of success, are extremely few. The patient reported by Brunschwig¹ succumbed to local recurrence and hepatic metastases before leaving the hospital. Recently, a case of successful resection was reported by George Cile, Jr.,^{4, 5} and another has been added by Illingworth.⁹ Otherwise no claims of pancreatic head excision with recovery have been published to our knowledge.

Formidable anatomic barriers, chiefly the intimate fixation of the portal and the superior mesenteric vein to the pancreas, seem to preclude the likelihood of further technical advances in this field. In Brunschwig's case, resection appears to have been facilitated by the existence of an unusually mobile pancreas, a favorable circumstance which can rarely be found in the human subject. The operative descriptions of Cile and Illingworth would suggest that the amount of pancreatic tissue resected by each was small.

Thus, for the present at least, the surgeon must be content with measures which afford only symptomatic benefit to patients with carcinoma involving the head of the pancreas, and in most cases of ampullary malignancy as well. Essentially his efforts must be restricted to the relief of the resultant mechanical interference with excretion of bile and the accompanying severe organic changes and subjective manifestations of complete obstructive jaundice.

These patients, as a rule, are poor subjects for an extensive surgical procedure. They are usually at or beyond middle age. They are debilitated. They are enfeebled by the effects of progressive and profound cholemia, with its related physiochemical disturbances. They are liable to hemorrhage. They suffer from biliary infection, to a greater or lesser degree. The situation is analogous to intestinal or urinary tract obstruction. The immediate need is for relief of the obstruction. The procedure to be adopted should be one which effectively fulfills this purpose, with minimum risk.

Two types of palliative operations are available in dealing with carcinoma of the head of the pancreas. The choice of procedure lies between reestablishing bile flow into the intestinal tract by anastomosis or by providing biliary excretion through external drainage. Of these two measures, the former has been almost routinely adopted by most surgeons when palliation has been sought.

It has been our impression for some time that biliary-intestinal anastomosis, as a primary procedure, is rarely warranted in these cases. This opinion has been formed through personal experiences and from critical review of the published results of other observers. The high immediate operative mortality rate associated with internal drainage of the biliary tract does not appear to justify its routine employment.

For these reasons, during the last two years (1938 and 1939), it has been our practice to provide only gallbladder or common duct drainage as the initial surgical step in most cases of complete obstructive jaundice due to chronic pancreatic disease. The purpose of this communication is to review this subject in the light of our experience and particularly to compare the results obtained with external drainage as opposed to internal biliary decompression. These two methods will be judged chiefly with regard to operative mortality, symptomatic relief, and length of postoperative survival.

Published statistics dealing with mortality rates in palliative operations for carcinoma of the head of the pancreas are not encouraging. They deal chiefly with the procedure of primary biliary-intestinal anastomosis. The immediate mortality rate averages between 30 and 50 per cent. Hunt and Budd⁸ state that the mortality in anastomotic operations "approaches 70 per cent." Judd and Parker¹⁰ had 18 deaths in 34 cases of anastomosis in pancreatic carcinoma. Fraser's⁷ mortality rate, in a large compiled series, with primary cholecystogastrostomy, for malignant cases, was 51.8 per cent. Oppenheimer, Glass, and Netter¹² found a mortality rate of 44.1 per cent, with primary internal drainage. Eliason and Johnson⁶ had an operative mortality of 40 per cent, with cholecysto-enterostomy. Somewhat lower are the figures of Cohen and Colp,² 32 per cent, Zollinger and Kevorkian,¹⁹ 31 per cent, and Ransom,¹⁵ 29.17 per cent. The former found a greater mortality with simple abdominal exploration alone, than with anastomosis, which would suggest that side-tracking of the biliary flow was reserved for the less desperate cases. The lowest reported mortality is that of Coller and Winfield,³ 26 per cent, but their series included a large proportion of cases in which the biliary obstruction was due to stone and other benign lesions.

The only available data comparing the operative mortality rates of external with internal drainage of bile for obstructive jaundice due to chronic pancreatic disease is that given by Fraser⁷ who found an operative mortality rate of only 11.6 per cent in 84 cases of surface drainage, and 24 per cent in anastomosis performed after initial biliary decompression. In the same collected series, the immediate operative mortality rate with primary cholecystogastrostomy for pancreatic malignancy was 51.8 per cent. The contrast is striking.

and merits consideration. Walters,¹⁶ some years ago, also called attention to the advisability of delayed anastomosis but gave no data in his paper.

A striking uniformity is found in the postoperative survival period of these cases as reported by various authors. Palliative procedures, while materially adding to the comfort of patients with carcinoma of the head of the pancreas, have little effect in prolonging life expectancy. Most patients succumb within six months after operation, few are alive after one year. The average duration of life postoperatively, even allowing for rare instances of unusually long survival, is between seven and eight months. Fraser, in his series, found 66 per cent dead under six months, and 90 per cent within 12 months. The average survival periods reported by other authors are as follows: Zollinger and Kevoikian, 9 months; Judd, 7.3 months; Lahey,¹¹ 8.6 months; Collier and Winfield, 7.2 months; Eliason and Johnson, "short"; Oppenheimer, Glass, and Netter, 7 months. Oppenheimer¹³ reported one unusual instance of long postoperative survival (29 months).

Findings—During the ten-year period (1930–1939 inclusive), 106 patients were operated upon on the Surgical Ward Services of the Mt. Sinai Hospital, with the diagnosis of carcinoma of the head of the pancreas. The mortality rate for the entire series was 33 per cent (35 operative deaths in 106 cases). Biliary-intestinal anastomoses were performed in 50 of these patients, with 24 deaths, an operative mortality rate of 48 per cent. In contrast to these high figures, 27 patients had external biliary drainage, alone, as the primary operative procedure, with three deaths, a mortality rate of only 11.1 per cent. In the remaining 29 cases of this series, operation was limited to abdominal exploration. In this group, there were eight deaths with a mortality rate of 27.5 per cent. These findings are tabulated in Table I.

TABLE I

	No. of Cases	No. Died	Mortality %
Total	106	35	33
Anastomosis	50	24	48
External drainage	27	3	11.1
Celiotomy only	29	8	27.5

In the latter two years of this study, primary anastomoses were reserved for the younger, incompletely-obstructed and better risk cases. For the others, a careful routine of preoperative preparation, minimal operative manipulation, and subsequent care was followed. Operation was withheld for several days to permit administration of fluids and improvement of liver function. Most patients received one or more transfusions of fresh citrated blood. All were given bile salts and vitamin K orally.

The operations were performed under local novocain anesthesia, through a short subcostal incision. Exploration was limited to steps essential for confirmation of the diagnosis of noncalculous obstruction. When the gallbladder was found distended, and the pancreatic head enlarged, by digital examination, cholecystostomy was performed without exposure of the pancreas and without attempting to obtain a biopsy specimen. The common duct was drained

by T-tube in those patients where the gallbladder was absent due to previous operation

Two or three weeks after operation, visualization of the biliary tract was obtained by roentgenographic study following injection of lipiodol through the cholecystostomy tube. This was done to guard against the possibility of overlooking common duct or ampullary stones and to reveal the site and degree of obstruction due to extrinsic pressure.

The patients were discharged from the hospital with the drainage tube left indwelling. Bile salt therapy was continued. They were seen periodically for follow-up examinations. In the instances where good general condition was maintained after four months, lipiodol studies were repeated. When complete common duct obstruction persisted, though the patient remained well and continued to gain weight and strength more than six months after operation, it was assumed that the diagnosis of pancreatic malignancy was probably incorrect. These patients were returned to the hospital for further study and reoperation. They were now in far better condition for abdominal exploration, and possible anastomosis, than at the time of the original drainage.

During this period of study, operation was performed upon 28 patients with obstructive jaundice due to chronic pancreatic disease. There were five deaths, giving a total mortality rate of 17.8 per cent. Cholecystostomy or choledochostomy, or both, were carried out in 16 of these cases with two deaths (12.5 per cent). There were three deaths in eight instances of biliary-intestinal anastomosis, a mortality rate of 37.5 per cent. Four patients had celiotomy only. The contrast with the preceding period, in which primary anastomosis was performed in a majority of the cases, is demonstrated in Table II.

TABLE II

1930-1937	No. of Cases	No. Died	Mortality %
Total	78	30	38.4
Anastomosis	42	21	50
External drainage	11	1	9.1
Celiotomy only	25	8	32
1938 and 1939	No. of Cases	No. Died	Mortality %
Total	28	5	17.8
Anastomosis	8	3	37.5
External drainage	16	2	12.5
Celiotomy only	4	0	0

Late follow-up records were available in 62 of the 71 patients who survived and left the hospital after operation. Only nine are known to be alive at the present time, the remaining 53 having succumbed to carcinoma at varying times, usually within a few months postoperatively. These findings are shown in Table III.

The life expectancy of these patients is brief. Over 80 per cent are dead within one year after operation. The average survival period is only 5.5 months. It is not materially influenced by the type of palliative procedure em-

ployed The few instances of prolonged survival may generally be regarded as nonmalignant cases

Analysis of Findings—It is evident that anastomosis between the biliary and intestinal tracts in the presence of complete obstructive jaundice is an undertaking of great hazard It invites an operative mortality rate of nearly 50 per cent This in contrast with a mortality rate of only 10 to 12 per cent for external biliary drainage The benefit to the patient as regards relief of discomfort and length of postoperative survival period is about the same with either procedure The disparity between the relative risk of internal as opposed to external drainage is striking (51)

A case report is given to illustrate the advantage of delayed anastomosis

TABLE III

LENGTH OF POSTOPERATIVE SURVIVAL				
	Biliary- Entero- anastomosis	External Drainage	Exploratory Celiotomy	Total
No Followed	25	18	19	62
Died				
Under 6 mos	16 (64%)	7 (38.8%)	12 (63.2%)	53 (85.5%)
6-12 mos	6 (24%)	4 (22%)	5 (26.3%)	
1-2 yrs	1 (4%)	1 (5.5%)		
Over 2 yrs	1 (4%)			
Average survival period	6.3 mos	6.1 mos	5.1 mos	5.5 mos
Alive	1 at 1 yr	4 over 1.5 yrs	1 over 5 yrs	9 (14.5%)
		2 at 8 mos	1 at 3.5 yrs	

Case Report—Hosp No 435647 J S, male, age 51, was admitted to the hospital, February 1, 1939, having been ill for seven weeks with mild, upper abdominal discomfort, progressively increasing jaundice, and the loss of 17 pounds in weight He appeared much older than his age, feeble and deeply icteric A globular mass was palpable beneath the liver edge His stools were clay-colored The urine contained much bile, and only a trace of urobilin Blood cholesterol was 400 mg per cent, cholesterol 280, and the icterus index 38

This patient presented a grave risk for primary cholecystogastrostomy Cholecystostomy was performed with minimal exploration He gained rapidly postoperatively His jaundice cleared promptly He was discharged six weeks after the first operation, with a biliary fistula and followed as an out-patient

Eight months later his condition was excellent, despite persistence of complete common duct obstruction It was felt that he might have chronic pancreatitis rather than carcinoma He was readmitted to the hospital, and secondary cholecystogastrostomy was performed, October 15, 1939 Convalescence was uneventful When seen over one year after his initial operation, he was symptom-free and had regained his maximum weight His operative wound was healed, his stools were brown, and his general condition good

COMMENT—Attempts to restore continuity of bile flow into the intestinal tract by anastomosis with the gallbladder or common duct, in the presence of obstructive jaundice due to carcinoma of the pancreas have resulted, consistently, in a high percentage of operative deaths Of those who survive operation, the average life expectancy is only a few months

Reestablishment of bile flow into the intestinal tract is of little practical importance It does not lengthen the survival period nor add materially to the comfort of the survivor beyond results obtained by the surface drainage

of bile. The oral administration of bile salts and vitamin K adequately compensates for lack of bile in the bowel. Palliation can be as effectively accomplished in these cases by the relatively simpler and less hazardous procedure of creating an external biliary fistula through cholecystostomy or choledochostomy.

SUMMARY AND CONCLUSIONS

(1) Radical excision of carcinoma involving the head of the pancreas is rarely possible.

(2) The choice of palliative procedure lies between biliary-intestinal anastomosis and external biliary drainage.

(3) In our series, primary anastomosis resulted in an operative mortality rate of 48 per cent (24 deaths in 50 cases).

(4) Contrasted with this high figure was a mortality rate of 11.1 per cent when the initial operation was restricted to external drainage alone (27 cases with three deaths).

(5) Symptomatic improvement and the postoperative survival period in the externally drained cases was as good as with anastomosis.

(6) An operative procedure which carries a mortality risk of almost 50 per cent does not seem warranted when the survivors can expect to live only a few months after operation.

(7) Since chronic pancreatitis cannot, with certainty, be differentiated from carcinoma even at operation, those patients who might otherwise survive if simple biliary decompression were instituted are sometimes subjected needlessly to the same risk as cancer patients.

(8) It is recommended that, except in the rare cases of young patients in good general condition, noncalculous, complete obstructive jaundice be treated surgically by simple decompressive operation alone, as the initial operative procedure.

(9) Those patients who are alive and in good condition more than six months after operation may be assumed to have benign rather than malignant lesions of the pancreas.

(10) If common duct obstruction persists, they can then be operated upon again with relative safety, and the continuity of bile flow into the intestinal tract restored.

(11) This procedure has been followed on our service at the Mount Sinai Hospital during the last two years with encouraging results.

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ILEUS FOLLOWING FRACTURED RIBS

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FRACTURE OF RIBS complicated by paralytic ileus is rare. We have been able to find only five cases reported to date. Adams¹ described the first two in 1910, Ralphs² cited the third in 1925, and Vandell³ reported the fourth in 1926. Christopher,⁴ in 1929, summarized the previously reported four cases and added the fifth.

The rarity and severity of this complication when it does occur, make this condition interesting and worthy of study. Among the 454 cases of fractured ribs seen at the Henry Ford Hospital during the past 24 years, there have occurred 10 cases of paralytic ileus complicating the injury. Only cases of fractured ribs uncomplicated by conditions such as pneumonia, fractured pelvis, or fractured vertebrae, which are known to produce ileus, are included in this study. Brief reports of these cases follow.

CASE REPORTS

Case 1—J. T., white, male, age 31, while riding a motorcycle, collided with a car December 2, 1926. He was brought to the Henry Ford Hospital immediately. Roentgenologic examination showed fractures of ribs 8, 9 and 12 on the left side, 5 cm from the lateral margin of the vertebral column. There were no abdominal symptoms. Leukocytes 15,200, with 79% polymorphonuclear cells. On December 5, 1926, marked abdominal distention developed and persisted for two days, being treated conservatively with hot water bottles to the abdomen, enemata and cathartics. The distention gradually disappeared, and his course was uneventful. He was discharged December 14, 1926.

Case 2—D. D., white, female, age 54, tripped and fell across a bucket February 6, 1933, striking her left chest. She was taken immediately to the Henry Ford Hospital and roentgenologic examination revealed fractures of ribs 10, 11 and 12 on the left side, 10 cm from the lateral vertebral border. There were no signs or symptoms pointing to any intra-abdominal injury. Marked distention developed which was treated with enemata and insertion of a rectal tube. It subsided completely in 36 hours.

Case 3—T. C., white, male, age 32, was struck by an automobile May 12, 1935, and was admitted to another hospital. On May 14, 1935, he was transferred to the Henry Ford Hospital where roentgenologic examination showed fractures of ribs 3 and 4 on the right side, near their articulations with the spine, and fractures of ribs 5, 6 and 8 on the right side, at the posterior axillary line. There was also a fracture of the left humerus. On the day following admission abdominal distention associated with repeated vomiting developed. On May 16, 1935, the distention continued with the patient vomiting small amounts frequently. Gastric aspiration and lavage, repeated enemata, and multiple doses of pitressin and prostigmin were necessary to control the distention, which finally subsided on May 17, 1935. Convalescence was slow and he was discharged June 13, 1935.

Case 4—C. T., white, male, age 24, was injured in an automobile accident October 13, 1935. He was admitted to the Henry Ford Hospital on October 16, 1935, because of

pain in the left chest. There were no signs of any intra-abdominal injury. Leukocytes 10,100, with 84% polymorphonuclear cells. Roentgenologic examination revealed fractures of ribs 7, 8 and 9 on the left side, 15 cm from the lateral vertebral border, and fracture of the tenth left rib, 5 cm from the vertebral border. Moderate abdominal distention was noted October 18, 1935, which was treated conservatively, subsiding 24 hours later. Convalescence was slow because of the development of a traumatic pleurisy, and he was discharged November 25, 1935.

Case 5—J. Van H., white, male, age 55, was admitted to the Henry Ford Hospital December 17, 1936, because of abdominal distention, vomiting and constipation of 24 hours' duration. On December 15, 1936, he had fallen eight feet from a ladder, striking his chest on the back of a sofa. His physician had made a diagnosis of fractured ribs and had strapped his chest. Roentgenologic examination revealed fracture of the fourth rib on the left side, 2 cm from the vertebral border, and, also, fracture of the eleventh rib on the left side, 7.5 cm from the vertebral border. Treatment with numerous enemata and repeated doses of pitressin was effective. The abdominal distention subsided 3½ days after admission, and he was discharged December 22, 1936.

Case 6—W. D., white, male, age 41, was injured in an automobile accident January 3, 1938. He was given emergency treatment at a hospital in the vicinity, and was then transferred to Henry Ford Hospital. Roentgenologic examination showed fractures of ribs 3, 4, 5, 6, 7, 8, 9, 10 and 11 on the left side. The third rib was fractured in the axillary line, while the remainder were fractured 2.5 cm or less from the vertebral borders. The eighth and ninth ribs were also fractured in the posterior axillary line, and there was a comminuted fracture of the clavicle. Abdominal distention developed January 5, 1938, and was of marked severity the following day, but disappeared January 7, 1938. Treatment consisted of gastric aspirations, frequent enemata, and repeated doses of pitressin and prostigmin. His course was further complicated by the development of a saphenous phlebitis. He was discharged February 25, 1938.

Case 7—E. M., white, male, age 45, fell 15 feet, striking his left chest May 17, 1938. He was admitted directly to the Henry Ford Hospital in shock. Roentgenologic examination revealed fracture of the ninth rib 5 cm to the right of the vertebral column, of the tenth right rib, which was markedly comminuted near its articulation, and of the eleventh right rib 5 cm from the vertebral border, with marked comminution. The seventh and ninth ribs on the right side were fractured in the anterior axillary line. A tension pneumothorax developed, and was treated with an intercostal tube leading to a water-seal. Abdominal distention appeared 48 hours after the accident and persisted for two days, gradually subsiding under treatment with frequent enemata and repeated injections of pitressin and prostigmin. He was discharged June 17, 1938.

Case 8—A. J., white, male, age 58, was admitted to the Henry Ford Hospital May 19, 1939, after he had slipped and struck his right chest when getting out of the bath tub. Roentgenologic examination showed fracture of ribs 6, 7 and 8 on the right side, in the midaxillary line, and fractures of the tenth and eleventh, 3 cm to the right of the vertebral border. Abdominal distention developed May 21, 1939, and he was treated with enemata, subsiding in 24 hours. He was discharged May 22, 1939.

Case 9—G. B., white, male, age 40, was injured in an automobile accident November 2, 1939, and 11 hours later he was admitted to the Henry Ford Hospital. The abdomen was moderately distended on admission. Roentgenologic examination showed fracture of the third rib on the right side in the midaxillary line, and fractures of ribs 3, 4, 5 and 6 on the left side, in the midaxillary line. Abdominal distention persisted from the time of admission until November 6, 1939. Treatment consisted of repeated enemata, injections of pitressin, and the introduction of a rectal tube. Continuous oxygen was administered from November 2, to November 12, 1939. He was discharged November 23, 1939.

Case 10—J. M., white, male, age 48, was injured March 28, 1940 when his chest was caught between a steel box and a door-jack. He was unconscious for a short period following the accident. Roentgenologic examination revealed fractures of ribs 5, 6 and 7

on the right side, in the midaxillary line, and a second fracture of the sixth rib, 2 cm to the right of the vertebral border. Abdominal distention appeared 24 hours after the accident, and persisted for two days. Numerous enemata, and repeated injections of pitressin and prostigmin effectively controlled the distention. A flat film of the abdomen showed dilated loops of small and large intestine. The patient was discharged April 6, 1940.

TABLE I

DISTANCE OF FRACTURE SITE FROM VERTEBRAL MARGIN AS SEEN ROENTGENOLOGICALLY

Case	Sex	Ribs Fractured	Side	Distance from Vertebral Margin
1 (86697)	M	8 9 and 12	L	5 cm
2 (6763)	F	10 11 and 12	L	10 cm
3 (212352)	M	3 4 5 6 and 8	R	3-4 cm
4 (224589)	M	7 8 and 9	L	1 5 cm
		10	L	5 cm
5 (58476)	M	2	L	2 cm
		11	L	7 5 cm
6 (268379)	M	2	L	11 cm
		4 5 6 7 8 9, 10	L	2 5 cm
		8 and 9	L	11 5 cm
		11	L	0 5 cm (comminuted)
7 (275227)	M	7 and 8	R	Anterior axillary line
		9 and 11	R	5 cm
		10	R	0 5 cm (comminuted)
8 (292902)	M	6 7 and 8	R	Midaxillary line
		10 and 11	R	3 cm
9 (184866)	M	2	R	Midaxillary line
		3 4 5 and 6	L	Midaxillary line
10 (309371)	M	6	R	2 cm
		5 6 and 7	R	Midaxillary line

NOTE: Since it is impossible to measure accurately the fracture site beyond the axillary line on the roentgenogram, measurements beyond this point are not given.

An analysis of these cases (Table I) shows that eight out of ten (80 per cent) had one or more fractured ribs within 5 cm of the lateral vertebral border. In two instances the head of the rib was badly comminuted. It is notable that all of these cases, except one, were males. The five previously reported cases were also males. The ages varied from 24 to 58 years, the average being 46.8.

The abdominal distention appeared ten to 84 hours after the injury (Table II).

TABLE II

THE TIME OF ONSET OF THE ILEUS IN THE PRESENT SERIES OF TEN CASES

Number of Cases	Time of Onset (Hours)
2	10-12
3	13-24
1	25-48
3	49-72
1	73-84

The ileus that occurred was paralytic in type, and varied in severity. The distention lasted from one to six days, and in eight cases the duration was two or more days. As soon as the distention was noted, energetic treatment for its control was promptly started. This usually consisted of close observation, repeated enemata, use of the rectal tube, and doses of pitressin or prostigmin at intervals of one or two hours. In three cases gastric aspirations and lavage were necessary.



Case No 6

Case No 7

FIG. 1.—Reproductions of roentgenograms illustrative of paravertebral fractures

Although five of the cases had a prolonged convalescence and period of hospitalization greater than 25 days, all of the patients recovered under this treatment without operation. We believe that if the presence of a ruptured intra-abdominal viscus can be ruled out, as it was in these ten cases, this type of patient is best treated conservatively without operation. The difficulty arises in the differential diagnosis between this type of reflex paralytic ileus and distention secondary to intra-abdominal injury. The upper abdominal muscle spasm secondary to irritation of the lower intercostal nerves by the fracture adds to this difficulty.

Discussion—In Figure 2, it is seen that the thoracic portion of the ganglionated sympathetic cord is situated on the heads of the ribs beneath the parietal pleura and just lateral to the bodies of the thoracic vertebrae. The three splanchnic nerves arise from the lower portion of the thoracic cord and are distributed to structures in the abdominal cavity. The great splanchnic nerve arises by a series of roots from the fifth to the ninth ganglia inclusive. The small splanchnic arises from the ninth and tenth, or tenth and eleventh

ganglia or from adjacent portions of interganglionic cords. The least splanchnic arises from the lowest of the thoracic ganglia and may receive a filament from the small splanchnic, from which it occasionally takes origin. Rarely, a fourth splanchnic nerve is formed by filaments from the cardiac nerves aided by twigs from the lower cervical and upper thoracic ganglia. The efferent splanchnic fibers, after passing through the ganglionated cord, are distributed below the diaphragm as visceroinhibitory fibers to the stomach and intestine, motor fibers for a portion of the circular muscle of rectum,

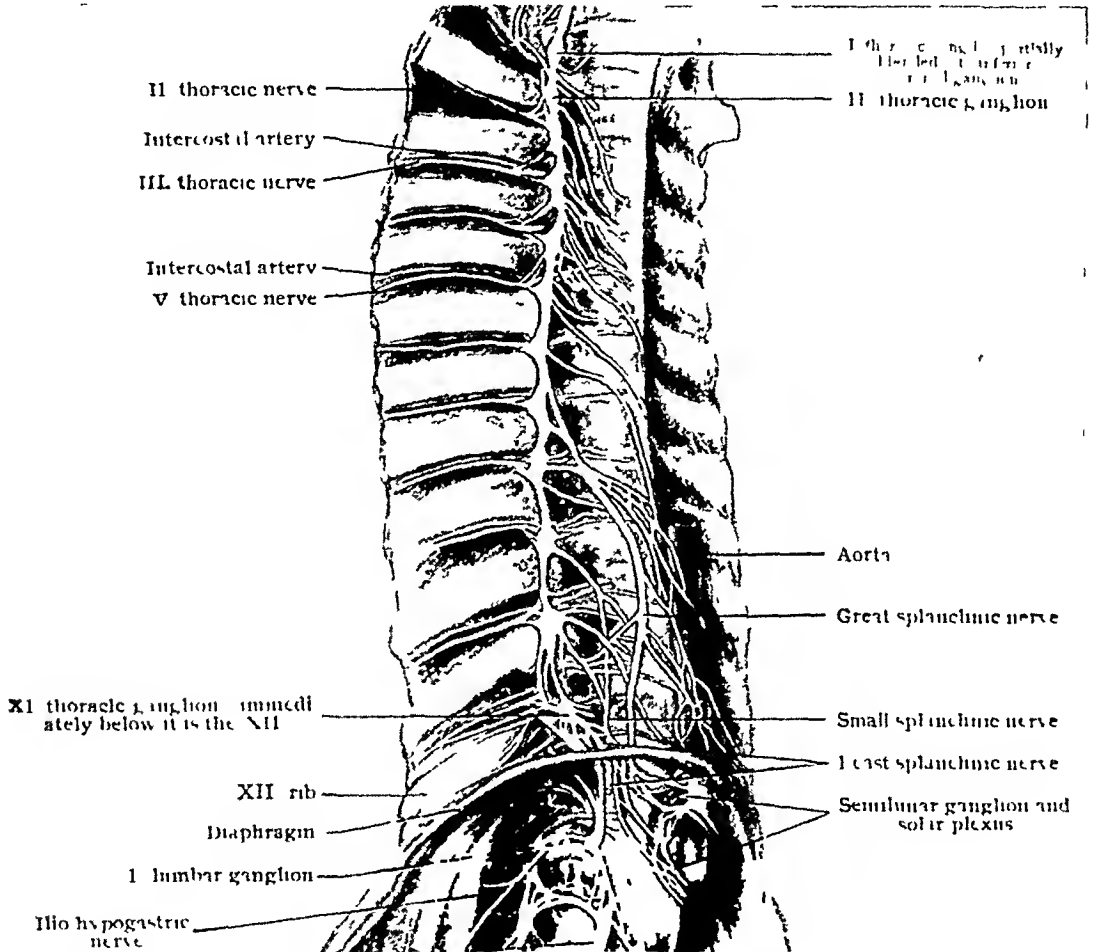


FIG. 2—Showing the thoracic portion of the ganglionated sympathetic cord and the splanchnic nerves (Human Anatomy Piersol, J. B. Lippincott Co. Philadelphia, 5th Edition, 1916)

vasomotor fibers for the abdominal aorta and its branches, and secretory and sensory fibers for the abdominal viscera. The vagus and splanchnic nerves act as antagonists to each other, the vagus being motor and the splanchnics inhibitory in action. Division of the splanchnics causes marked increase in the intestinal movements, while stimulation of the splanchnics causes a cessation of movements and relaxation of the small bowel (Bayliss and Starling,⁶ Macleod⁷). Chemical or electric stimulation of the splanchnics leads to distention and paresis of the entire small intestine.⁸ It is evident then that the sympathetic ganglia, resting on the heads of the corresponding ribs, give rise to the splanchnic nerves which supply inhibitory fibers to the stomach and

intestine Artificial stimulation of the splanchnic nerve produces relaxation and cessation of movement of the small bowel

The mechanism by which paralytic ileus is produced by fracture of one or more ribs is not clearly understood Adams¹ believed that some displacement of the proximal portion of the fractured rib occurs, producing irritation of the sympathetic chain of the thoracic ganglia and the splanchnic nerves arising from them Vandel³ believed that, anatomically, it was difficult to understand how the proximal rib fragment, which is strongly bound to the vertebral column by ligaments, could move to the extent necessary for this explanation to apply, although the point of fracture in his case was one inch to the right of the vertebral border Morton⁸ states that the traumatic effects are supposed to be reflex through the peripheral nerves to the sympathetic ganglia stimulating the sympathetics Eight out of our ten had one or more rib fractures within 5 cm of the lateral vertebral border, and in two instances the actual head of the rib was comminuted From a study of these cases we believe there are four possible means of splanchnic stimulation

(1) Irritation of the sympathetic thoracic ganglia and, therefore, the splanchnic nerve may occur through some displacement of the proximal rib fracture segment as first suggested by Adams¹ At least in those cases in which the head of the rib was comminuted, it is evident that sufficient displacement could occur

(2) Edema of the tissues adjacent to the point of fracture may encroach upon the position of the thoracic sympathetic ganglia

(3) Reticopleural hematoma in the vicinity of the thoracic sympathetic ganglia or splanchnic nerves resultant from the trauma may produce pressure on the sympathetic ganglia and splanchnic nerves Demel⁹ has shown that an experimentally produced hematoma in the region of the splanchnic nerve causes a paresis and a meteorism of the entire small bowel

(4) Stimulation of the peripheral nerves either intercostal or abdominal may result in reflex stimulation of the splanchnics through the thoracic ganglia, as suggested by Ralphs² This, possibly, would explain the development of ileus after rib fracture located some distance from the spine Olivecrona¹⁰ noted that strong sensory stimuli, such as crushing of the testes, produce a powerful inhibition of peristalsis by reflex stimulation of the splanchnics If the splanchnics are divided, this reflex inhibition of peristalsis will not occur Another example of dilatation of the stomach and small intestine caused by reflex stimulation of the splanchnics is seen in the abdominal distention occasionally seen with renal colic (Eisendrath¹¹)

SUMMARY AND CONCLUSIONS

(1) Intestinal ileus following fractured ribs is a rare condition, to date only five cases have been reported

(2) Ten additional cases of ileus complicating fractured ribs are described

(3) The mechanism by which this dilatation of the small bowel occurs is not clearly understood

(4) Irritation of the dorsal sympathetic ganglia and splanchnic nerves appears to be the most plausible explanation. This irritation may be accomplished by displacement of the head of the rib or a proximal fragment, retropleural edema or hematoma in the paravertebral area, or reflex stimulation of the splanchnics through the peripheral abdominal or thoracic nerves.

(5) Experimental stimulation of the splanchnic nerves produces relaxation and cessation of movement of the small bowel.

(6) In eight of ten cases of ileus following rib fracture, the fracture was within 5 cm of the lateral vertebral border. This proximity to the thoracic sympathetic ganglia and splanchnic nerves suggests that irritation of these nerves as a result of trauma does occur.

(7) If the presence of a ruptured intra-abdominal viscus can be ruled out, this condition is best treated conservatively without operation.

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THE EFFECT OF THE SULFONAMIDES ON THE PREVENTION OF EXPERIMENTAL BRAIN ABSCESS

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BUCY,¹ GRANT,² AND ROWE³ have used the sulfonamides in the treatment of brain abscesses as an adjunct to surgical therapy. Clinical data suggested that when these compounds are used the incidence of meningitis is reduced and the spread of the encephalitis following operation may perhaps be controlled. In the present communication we are reporting on the use of the sulfonamides in the prevention of the experimental brain abscesses.

Experimental Method—Healthy mongrel dogs were used in these experiments. In the present studies the technic for abscess production was the same as previously reported,⁴ except that the dose of bacterial inoculum was increased. This was done to insure death of the control dogs within a short period (24 to 72 hours), following introduction of the organisms.

At the start of this experiment one of the sulfonamides, sulfapyridine, was administered through various channels: (1) Intravenous injection of 0.1 Gm. per kilogram of the sodium salt, twice a day, (2) the daily intravenous injection of 0.1 Gm. per kilogram of the sodium salt and the introduction intraperitoneally of 0.4 Gm. per kilogram of an emulsion of sulfapyridine prepared by the use of sonic vibrations⁵, and (3) 0.5 Gm. of sulfapyridine per kilogram by mouth daily given in a single dose.

Blood was withdrawn each morning before giving an additional dose of the drug, and determinations were made on these samples of the blood concentration of the drug being used. The oral administration was found to give the most satisfactory results and was used in most of the experiments. The dose of sulfanilamide, sulfapyridine, and sulfathiazole was 0.5 Gm. per kilogram daily, and that of sulfadiazine 0.25 Gm. per kilogram daily. All of these compounds were started two hours following the cerebral injection of the bacterial inoculum unless otherwise stated. All treated dogs received a course of five days of treatment.

Sulfanilamide, sulfathiazole, sulfapyridine, and sulfadiazine were used against pneumococci Type-III, hemolytic streptococci and *Staphylococcus aureus*. The organisms were obtained from the heart blood of living mice and were cultured for 12 hours. Control experiments were carried on simultaneously with each chemotherapeutic experiment.

Results—The data on mortality and survival obtained in these experiments are given in Table I. It can be seen that when the bacterial inoculum consisted of pneumococci, sulfapyridine and sulfadiazine provided complete protection against abscess formation when chemotherapy was begun two hours

following injection of the bacterial inoculum Sulfapyridine protected 75 per cent of the dogs from abscess formation even though therapy was not begun for 17 hours following the injection of the bacterial inoculum The mortality of the control groups was 100 per cent While sulfanilamide protected 66.0 per cent of the dogs, sulfathiazole was only moderately effective

Sulfapyridine was not used following the injection of *Staphylococcus aureus* When this organism was injected, sulfanilamide, surprisingly, seemed slightly more effectual than the other compounds which were used

TABLE I

Drug	Pneumococcus Type-III		Staphylococcus Aureus		Hemolytic Streptococcus	
	No. in Group	Per Cent Survival	No. in Group	Per Cent Survival	No. in Group	Per Cent Survival
Sulfanilamide						
Treated	6	66.0	4	100.0	4	75.0
Control	4	0.0	4	0.0	4	25.0
Sulfapyridine						
Treated	12	100.0			10	20.0
	4	75.0*				
Control	12	0.0			10	0.0
	4	0.0				
Sulfathiazole						
Treated	6	33.0	4	75.0	4	75.0
Control	4	0.0	4	0.0	4	25.0
Sulfadiazine						
Treated	7	100.0	4	75.0	4	50.0
					8	37.5†
Control	3	0.0	4	0.0	4	0.0
					4	0.0

* Treatment began 17 hours after inoculation

† Treatment began six hours after inoculation No latent abscesses have developed, and some dogs have lived six months

Sulfapyridine and sulfadiazine were less effectual against the formation of abscess where hemolytic streptococci were used than the other compounds, although sulfadiazine provided some protection even when therapy was begun as late as six hours following injection of the bacterial inoculum

In Chart 1 are recorded the mean blood levels of the drugs of the treated dogs during the first four days of therapy It is interesting to note the high mean levels which were maintained when sulfadiazine was used When sulfapyridine and sulfathiazole were administered orally a number of the dogs vomited at a variable period of time after the introduction of the drug into the stomach through a gastric tube This rarely occurred with sulfanilamide and never occurred with sulfadiazine

The mean blood concentrations of the treated dogs which died were in every instance within the range of the mean blood concentrations of surviving dogs, except for the dogs which died while receiving sulfadiazine Even so, these dogs maintained a mean blood concentration of 20.8 mg per cent until the time of death The minimal effective blood concentrations of these compounds were not determined

Discussion—The high sulfadiazine blood level was maintained on a

smaller dose per kilogram of body weight than any of the other sulfonamide compounds which were studied. The absence of low blood concentrations in any of the dogs which received sulfadiazine was, we believe, an expression of the ease with which this drug was tolerated when orally administered.

Comparison of the compounds shows that sulfanilamide and sulfadiazine are approximately equally effective for the organisms studied. The high blood level obtained when relatively small doses of sulfadiazine were used, and the complete absence of vomiting, would suggest that this compound may be the one of choice when oral sulfonamide therapy is indicated and close supervision is not possible. This would be especially true when these compounds were being administered immediately following injury during military engagements, where a considerable period of time may elapse before the injured man is admitted to a general hospital.

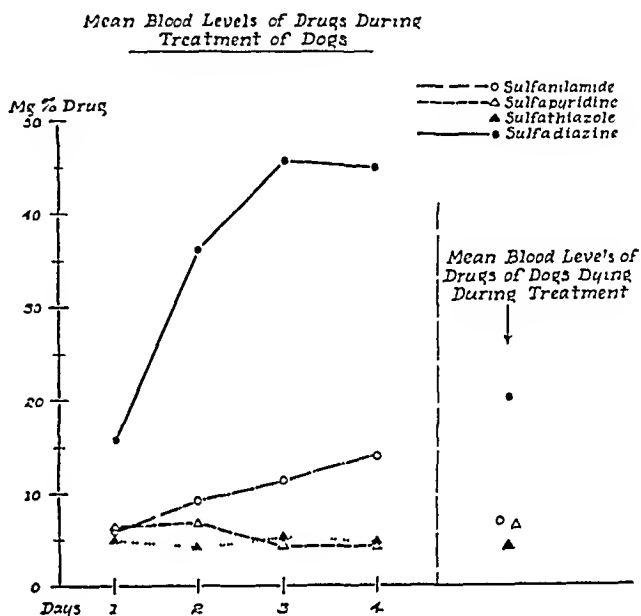
The data indicate that experimental cerebral infection can be prevented or controlled in a high percentage of instances with adequate oral sulfonamide therapy.

Conclusions—The data from these experiments indicate that sulfonamide therapy is effectual in preventing a pyogenic brain abscess following injection of pneumococcus Type-III, *Staphylococcus aureus*, and the hemolytic streptococcus into a cerebral area previously traumatized.

Sulfonamide therapy should be begun early, for the few data available suggest that with an increasing time interval between infection and the beginning of therapy the mortality also increases.

Sulfanilamide and sulfadiazine were found to be the most effective compounds.

It is suggested that intracranial infection in man, following injury, may, in part, be prevented by early and adequate sulfonamide therapy.



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THE RELATION OF HYPERTHYROIDISM TO HYPERTENSION*

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OMAHA, NEBR

A DISCUSSION of the relation of hyperthyroidism to hypertension was presented in a previous publication ² The opinions expressed in that discussion were derived from a study of a total series of 265 cases of hyperthyroidism, in which 80 cases, or 30 per cent of the series, had preoperative resting systolic pressures in excess of 150, that is, in excess of a level assumed to be the upper limit of normal

It is the purpose of the current communication to supplement the previous one with a report of an analysis of an additional 86 cases, 19, or 22 per cent, of which had resting systolic pressures in excess of 150

Since the analytical study showed that this second series differed little from the first one, the two are discussed jointly as a single combined series The sex-ratio was approximately four women to one man All cases had subtotal thyroidectomies, with preoperative records of essential data as summarized in Table I The average age was 35.5 years, the duration of toxic symptoms 12 months, and the basal metabolic rate plus 45.1 The preoperative blood pressures averaged 142/77 The systolic pressure exceeded 150 in 99, or 25 per cent of the cases, 160 in 65, or 18.5 per cent, and 200 in 13, or 3.7 per cent In general, the cases with the higher pressures were older and had had thyrotoxic symptoms for a longer time

TABLE I
DATA FROM ANALYSIS OF 351 CASES OF HYPERTHYROIDISM

	No of P t s	Per Cent of Total	Averages			B M R	Age of P t s	Duration of Toxic Symptoms (Mos)
			Systolic Pressure	Diastolic Pressure	Pulse Pressure			
Total cases studied	351		142	77	65	+45.1	35.5	12
Systolic over 150	99	25.3						
Systolic over 160	65	18.5	180	92	88	+41.5	43	24.5
Diastolic over 90	66	18.8						
Pressures over 150/90	52	14.8						
Pressures over 160/100	19	5.4	193	112.5	80.5	+36.2	47.5	27
Systolic over 200	13	3.7	228	111.5	116.5	+33	49	22.5

Assuming that 145 represents the upper limit of normal for the systolic blood pressure, all cases with pressures above this level were considered hypertensives, and follow-up observations one year or more after operation were obtained in all such cases which were available for examination Such records were obtained in 49 cases, or approximately one-half of the group A comparison of the resting blood pressure levels before and one year or more after operation is shown in Tables II and III

* Read before the first meeting of the Central Surgical Association, February 28, and March 1, 1941, Ann Arbor, Mich

The records of the 48 cases were tabulated in two groups (1) Those in which the preoperative systolic pressure was between 145 and 170, and (2) those in which it was 170 or more

In the first group there were 32 cases In 24, or 75 per cent, of these the systolic pressure one year or more after operation showed some reduction from the preoperative level, and in 19 of the 24, or 60 per cent of the

TABLE II
 ANALYSIS OF 32 CASES OF HYPERTHYROIDISM IN WHICH THE PATIENT HAD A PREOPERATIVE
 SYSTOLIC PRESSURE BETWEEN 145 AND 170

Age	Sex	Duration of Toxic Symptoms	Basal Metabolic Rate	Pathologic Condition	Preoperative Pressures		Pressures 1 Yr or More After Operation		Reduction		Increase	
					Sys-tolic	Diast-tolic	Sys-tolic	Dias-tolic	Sys-tolic	Dias-tolic	Sys-tolic	Dias-tolic
45	F	1 yr	+37	Adenohyperplasia	160	72	132	68	28	4		
18	F	1 yr	+55	Hyperplasia	155	100	119	83	36	17		
39	F	4 mos	+34	Carcinoma	160	100	122	78	38	22		
56	F	2 mos	+49	Adenohyperplasia	166	66	150	90	16			24
32	F	3 yrs	+46	Adenohyperplasia	160	106	115	70	45	36		
35	F	4 yrs	+75	Hyperplasia	150	95	130	70	20	25		
18	F	6 mos	+18	Hyperplasia	165	90	124	72	41	18		
22	F	4 yrs	+59	Adenohyperplasia	160	80	140	80	20	0		
46	F	3 mos	+28	Adenohyperplasia	160	90	168	100			8	10
38	F	4 yrs	+23	Adenoma	168	110	182	120			14	20
21	F	10 mos	+68	Hyperplasia	150	80	140	90	10			10
37	F	2 yrs	+17		145	100	180	100			35	0
62	F	5 mos	+91	Hyperplasia	150	70	150	68				
46	F	3 yrs	+23	Hyperplasia	150	90	126	82	24	8		
45	F		+41	Hyperplasia	155	80	126	80	29	0		
49	F	5 yrs	+94	Hyperplasia	156	70	170	90			14	20
33	M	2 mos	+36	Hyperplasia	150	70	146	82	4			12
57	F	1 yr	+33	Adenohyperplasia	158	78	140	100	18			22
24	F	3 yrs	+37	Adenohyperplasia	155	72	132	86	23			14
47	M	6 mos	+54	Hyperplasia	150	90	140	75	10	15		
35	F	2 yrs	+43	Hyperplasia	145	94	130	80	14	14		
22	F	2 yrs	+52	Hyperplasia	152	82	125	70	27	12		
34	F	3 yrs	+26	Adenohyperplasia	155	75	155	94			0	19
30	F	3 mos	+54	Hyperplasia	150	80	120	73	30	7		
56	M	3 yrs	+29	Adenohyperplasia	150	80	150	80	0	0		
25	M	4 yrs	+46	Hyperplasia	150	90	128	84	22	6		
36	M	3 mos	+60	Diffuse hyperplasia	160	95	140	90	20	5		
38	M	6 mos	+58	Diffuse hyperplasia	168	80	118	70	40	10		
48	M	10 mos	+48	Adenohyperplasia	154	95	160	100			6	5
60	F	14 mos	+32	Adenohyperplasia	170	105	150	100	20	5		
52	F	8 mos	+49	Adenohyperplasia	158	90	140	85	18	5		
45	M	2 yrs	+32	Diffuse hyperplasia	150	85	126	75	24	10		

group, there was considerable reduction, in 11 cases the pressure became normal There was a reduction of diastolic pressure in 17 cases Systolic pressure increased in five cases and diastolic pressure in ten cases There was no change of pressure in two cases

In the second group there were 16 cases (Table III) In eight of these, or 50 per cent, reductions of both the systolic and the diastolic pressure had

followed thyroidectomy and had been maintained for periods of one to five years. In four of the eight cases the pressure was nearly normal. In four cases there was an increase of pressure, in three of them an extreme increase. In two cases there was little or no change of pressure.

TABLE III
16 CASES OF HYPERTHYROIDISM WITH HYPERTENSION WITH
SYSTOLIC PRESSURE OF 170 OR MORE

Age	Sex	Duration of Toxic Symptoms	B M R	Pathologic Condition	Preoper B P		Postoper 1 Yr or More		Reduction		Increase	
					Syst	Diast	Syst	Diast	Syst	Diast	Syst	Diast
62	F	2 yrs	+28	Adenohyperplasia	250	120	180	80	70	40		
32	F	7 yrs	+78	Diffuse hyperplasia	200	100	120	72	80	28		
47	F	18 mos	+43	Adenoma	182	100	142	80	40	20		
25	F	1 yr	+63	Diffuse hyperplasia	178	80	65	50	113	30		
41	F	1 yr	+31	Adenohyperplasia	172	90	230	124			58	34
48	F	1 yr	+75	Diffuse hyperplasia	170	90	164	90	6	0		
26	F	6 mos	+25	Diffuse hyperplasia	170	90	130	85	40	5		
48	F	2 yrs	+51	Adenohyperplasia	170	90	210	100			40	10
56	M	2 yrs	+55	Adenohyperplasia	170	90	180	90			10	0
58	M	2 yrs	+48	Adenohyperplasia	180	110	130	90	50	20		
23	M	6 mos	+51	Diffuse hyperplasia	170	80	170	88			0	8
48	F	9½ mos	+60	Adenohyperplasia	230	140	210	140	20	0		
68	F	10 mos	+32	Adenohyperplasia	190	100	138	90	52	10		
52	F	1 yr	+45	Adenohyperplasia	240	160	200	130	40	30		
31	M	6 mos	+68	Diffuse hyperplasia	178	100	126	70	52	30		
49	M	14 mos	+44	Adenohyperplasia	182	115	210	120			28	5

Combining the figures from the two groups shows that in 21 cases the blood pressure was uninfluenced by relief of hyperthyroidism and either remained essentially unchanged or continued to increase. In 27, or a slightly larger number of cases, however, the blood pressure was appreciably reduced after thyroidectomy, and in 15 it became relatively normal or normal.

COMMENT—From the data just presented two types of cases are distinguishable:

(1) A type in which hyperthyroidism and an established hypertension co-exist, incidentally, in the same person as separate, unrelated entities. Usually, the hypertension is essential in type, although its severity apparently is increased by the thyrotoxic state, and some improvement may follow release from hyperthyroidism. Despite symptomatic improvement, however, the blood pressure, both systolic and diastolic, remains high and, usually, is not significantly lowered, and the hypertension continues to progress.

(2) A type in which relief of hyperthyroidism by subtotal thyroidectomy causes both the systolic and the diastolic pressure to recede promptly to a much lower, or normal, or nearly normal level, at which it remains or from which, after a period of many months, it again gradually ascends. This response suggests that thyrotoxicosis in these cases either is directly responsible for the hypertension or, more likely, precipitates or exaggerates a latent vascular disorder. It is conceivable that an inelastic or restricted vascular bed,

capable of receiving the normal cardiac output without appreciable elevation of blood pressure, would be unable to receive the increased output incident to hyperthyroidism without a sharp rise in the propelling force. Conversely, with lessening of the output by remission of hyperthyroidism the pressure required to propel the blood is diminished. In other words, this hypothesis assumes the existence of arteriolar pathologic changes which are insufficient to increase appreciably the resistance to a normal volume of blood flow but which are sufficient to prevent normal expansion as the load is increased in response to either hyperthyroidism, exercise, or the cold pressor test.

This hypothesis finds support in the response of the seven cases (three of the group in Table III, and four private cases not included in the present series) subjected to exercise and to the cold pressor test of Hines and Brown¹. These determinations are shown in Table IV. In all cases large reductions of blood pressure had developed and been sustained after subtotal thyroidectomy.

TABLE IV
EFFECT OF EXERCISE AND OF THE COLD PRESSOR TEST ON THE BLOOD PRESSURES OF SEVEN PATIENTS
ONE YEAR OR MORE AFTER SUBTOTAL THYROIDECTOMY

Case	Age	Preop B M R	Postop Pulse	Blood Pressure				Pulse Rate	
				Preop	Postop	After Exercise	After Immersion of Hands	After Exercise	After Immersion of Hands
1	47	+43	76	182/100	142/80	195/95	185/105	104	82
2	58	+48	84	180/110	130/90	190/100	185/105	110	92
3	62	+28	68	250/120	180/80	230/110	230/110	100	74
4	60	+62	82	210/110	150/105	220/112	218/110	98	80
5	56	+58	72	190/115	150/108	190/120	200/124	112	72
6	31	+68	72	178/100	126/70	160/90	148/90	92	82
7	45	+52	78	190/110	140/82	162/90	170/95	102	90

After the basal level of blood pressure had been obtained, each patient was given sufficient exercise to increase the pulse rate appreciably (from 16 to 40 beats per minute), and the blood pressure was determined immediately afterward and at subsequent intervals of 60 seconds. In each instance the pressure rose to the approximate preoperative resting level. Moreover, these levels were sustained abnormally long and receded abnormally slowly. Thus, the response of blood pressure to the increased cardiac output incident to exercise was approximately the same as that recorded preoperatively during the thyrotoxic state.

Each patient was then subjected to the cold pressor test described by Hines and Brown. In accordance with their technic, the lowest or basal level of blood pressure was obtained with the subject resting supine for 30 minutes or longer. With the blood pressure cuff in place on one arm, the opposite hand was immersed in ice water (4° C.) to a point just above the wrist for 60 seconds, and readings of blood pressure were made 30 and 60 seconds after the beginning of immersion. Within 30 seconds the pressure again mounted to approximately the same level which followed exercise. In the light of the

studies of Hines and Brown, the reaction of the blood pressure in these patients to the cold pressor test was excessive and abnormal, as is that in all subjects afflicted with essential hypertension. The studies of these investigators showed that in addition to the persons with hypertension there is a group of persons who do not have hypertension but do give excessive reactions to the cold pressor test. Persons in this group they designated "hyper-reacting normals," and they stated the belief that this excessive reaction indicates a latent quality and a likelihood of subsequent development of hypertension. On this basis it may be reasoned that my patients had potential if not real essential hypertension and that the latent factor had been precipitated or exaggerated by thyrotoxicosis.

It is interesting that in each of these seven cases there was a familial history of hypertension.

CONCLUSIONS

(1) As a physiologic response to hyperthyroidism, the systolic blood pressure is usually slightly elevated. It recedes to the normal level with relief of hyperthyroidism.

(2) In this series of 351 cases, hyperthyroidism was associated with unquestionable essential hypertension (systolic pressure above 170) in approximately eight per cent, and with elevations of the systolic pressure above the physiologic level (above 150) in 25 per cent. On the basis of changes of blood pressure following relief of hyperthyroidism, two types of cases are discernible. (A) Cases with fixed or established essential hypertension, in which the blood pressure and the course of the vascular disease are not significantly influenced by relief of hyperthyroidism, and (B) cases with latent or labile essential hypertension, in which the blood pressure shows considerable reduction after relief of hyperthyroidism or approaches a normal level and maintains this level for a period of months or years. In many cases of the second type the pressure is observed subsequently to ascend. In these cases there is excessive response in blood pressure to exercise and to the cold pressor test of Hines and Brown. It is suggested that the relation of hyperthyroidism to hypertension in these cases is provocative, and that hyperthyroidism merely precipitates or exaggerates hypertension which is latent.

It is further suggested that in both types there is arteriolar disease, differing only in degree. In the first type the disease is more advanced, rendering the vascular bed inadequate for even a normal volume of blood flow. In the second type the disease may be designated as pretensive hypertension which progresses to the condition of the first type with the advance of time.

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METASTATIC TUMORS IN THE BREAST

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No DISEASE is more full of surprises and less amenable to tradition than malignant tumors. They defy any classification or precedent. Hence the importance of continuing clinical investigation and reporting new phenomena.

Tumors of the breast are universally accepted as being primary in origin. This clinical observation is in accordance with the teaching of Virchow, that organs which are frequently the site of primary tumors are seldom affected by metastatic growths.

That metastatic tumors in the breast do occur was shown by Dawson,¹ in 1936, when he reported a case of gastric carcinoma with metastases to both breasts, proven histologically from autopsy material. He tabulated a series of ten cases collected from the literature. There have been no other reports of metastatic tumors of the breast up to the present writing.

Dawson confines metastatic mammary tumors to "those recorded instances where clinical and microscopic data point more or less to primary growths in another site."

Two such proven cases were admitted to the Brooklyn Cancer Institute. One case had its origin in an hypernephroma, the other, in a melanoma of the right forearm.

CASE REPORTS

Case 1—Hosp No 1680. M. S., white, female, age 43, was admitted to the Brooklyn Cancer Institute, October 8, 1938, complaining of pain in the right side of the abdomen and loss of 20 pounds in three months. Four months previous to admission (June, 1938) she developed a cough with occasional bloody sputum. In July, 1938, she was treated for bronchitis and pleurisy. A short time later she developed pain in the right lower quadrant and was admitted to a private hospital where her appendix was removed. After ten days she was discharged. Two weeks later she reentered the same hospital, still complaining of pain in the right lower quadrant. At this time examination and roentgenologic studies revealed "neoplasm of the lungs, hydronephrosis, and ptosis of the right kidney." She was then referred to the Brooklyn Cancer Institute for roentgenotherapy.

Physical Examination—The patient was an emaciated, chronically ill female. Temperature 100° F, pulse 120, respiration 20, blood pressure 168/60. Both breasts were symmetrical, of moderate size, and slightly pendulous. The skin was smooth and freely movable. The nipples were of equal size, and were not retracted or inverted, they showed no discharge. Deep in the center of each breast a nontender, irregular, firm tumor was palpated, measuring about 3-4 cm in diameter, attached to the underlying structures and only slightly movable. The tumor in each breast appeared to be the same size and shape, and symmetrically placed in the center. There were no palpable nodes in either axilla or supraclavicular regions. The patient stated that the breasts "never bothered" her.

The heart was somewhat enlarged, an apical systolic and double aortic murmur

was present, which was transmitted to the vessels of the neck. The lungs showed dulness at both bases and right interscapular areas, with diminished tactile fremitus and breath sounds. A few scattered moist rales were present.

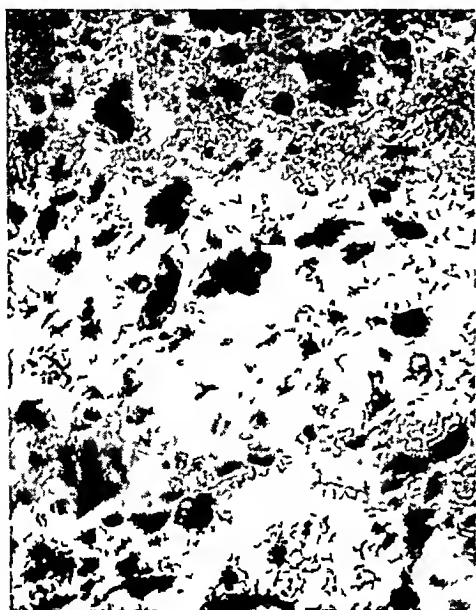


FIG 1—Case 1. Photomicrograph showing anaplastic cells of hypernephroma (×800).



FIG 2—Case 1. Photomicrograph showing anaplastic cells of metastatic hypernephroma in the breast (×800).



FIG 3—Case 1. Photomicrograph showing metastatic hypernephroma of the breast (×200).



FIG 4—Case 2. Photomicrograph showing metastatic melanocarcinoma of breast (×200).

The abdomen was slightly distended. The liver was enlarged to two fingers breadth below the costal margin. A large, firm mass was felt below the liver, corresponding to the region of the right kidney, which was very painful on palpation. There were no other palpable masses. The spleen was not enlarged. Pelvic examination revealed no evidence of pathology.

METASTATIC TUMORS IN BREAST

Roentgenographic examination of the chest showed multiple metastatic nodules in both lungs. A pyelogram showed a tumor of the upper half of the right kidney, associated with hydronephrosis. Urine Albumin 2 plus, with 43-61 red blood cells per field and many squamous epithelial cells. Blood chemistry Urea 36 mg, creatinine 1.2, sugar 100 mg. Blood examination Red cells 2,900,000, with 42% hemoglobin, white cells 33,000, with 84% polymorphonuclear leukocytes, 13% lymphocytes, and 3% eosinophils. Blood Wassermann, negative.

Both breast tumors were removed under local anesthesia for diagnosis. They were found to be histologically, the same—metastatic hypernephroma (Path No 1505). The patient received supportive treatment, but her condition became progressively worse and

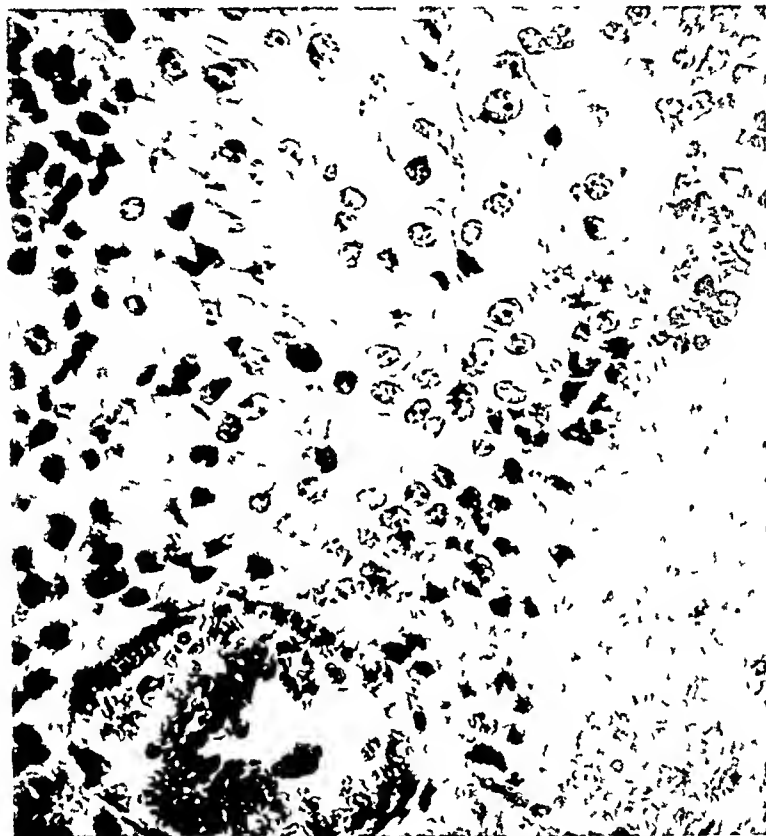


FIG 5—Case 2 Photomicrograph showing malignant characteristics of the cells (X800)

she died October 28, 1938. Autopsy was not permitted, except for removal of a portion of the primary tumor in the abdomen. The pathology of this tumor proved to be the same as that of the tumors of the breasts. Confirmation of this diagnosis was made by Dr. James Ewing. Both tumors proved to be of renal origin.

Case 2—Hosp. No. 7937. W. S., white, male, age 42, was admitted to the Brooklyn Cancer Institute, June 19, 1935, complaining of a lump on the right chest and right elbow. About two years previous to admission he had had a "wart" growth removed from the right forearm. About six months before admission he noticed a lump on the right elbow and right chest, which grew progressively larger. His family history and past history were irrelevant. He had lost ten pounds within the last year.

Physical Examination—The patient was a well-developed white male, weighing 158 pounds, and was 5' 5" in height. Not acutely or chronically ill. Temperature 99° F, pulse 80, respiration 18, blood pressure 120/90. A palpable node, the size of a walnut, was present in the right epitrochlear region. In the upper outer quadrant of the right mammary region was a large, firm tumor, the size of a grapefruit, extending from the upper part of the nipple to the anterior axillary line, and involving the lower outer two-thirds of the pectoral region. The skin over the tumor was stretched, but not adherent,

and the tumor appeared to be fixed to the pectoral muscles. The right nipple was somewhat larger than the left, freely movable, and without any evidence of gross pathology.

The heart sounds were regular in rate and rhythm, and no murmurs were heard. The lungs did not show any clinical evidence of pathology, but roentgenologic examination revealed a nodule, 2-3 cm in diameter, in the left lung, at the level of the fifth rib. The abdomen was free from any palpable tumor, but the liver was enlarged to 2 cm below the costal margin. This enlargement of the liver was also noted on a plain roentgenogram of the abdomen.

The blood chemistry and the blood count were within normal limits. The blood Wassermann was negative. The urine was not pathologic.

On July 11, 1935, a radical right mastectomy was performed, with excision of the epitrochlear node. The node was reported, by Dr. S. H. Polayes, as metastatic melanocarcinoma. The detailed gross and microscopic description of the breast by Dr. Polayes is as follows:

Pathologic Examination—Gross. Path No. 12366. "Specimen a section of breast with a triangular piece of skin, about 14 cm in greatest diameter, attached. It is also accompanied by pectoral muscle and fascia. The mass in the breast measures about 15 cm in greatest diameter, is lobulated and discolored dark brown except for a few projecting lobules which are gray in color and a few others of blue discoloration. The cut-surface presents areas of necrotic brown tissue. There is no direct continuity between the mass and the overlying epidermis.

Microscopic. "The breast tissue is the seat of discrete, fairly well-circumscribed areas of malignant epithelial cells, embryonal in character, many of which are filled with brown pigment. The tumor tissue cannot be traced to the breast structures. The ducts of the breast are distended and filled with large, pale cells of lacteal origin. *Pathologic Diagnosis.* Metastatic melanocarcinoma."

Various laboratory tests of the tumor extract were positive for melanoma.

The patient made an uneventful operative recovery, and was followed in the clinic until he died at his home in September, 1935.

SUMMARY

(1) Although tumors of the breast are universally accepted to be primary in origin, metastatic tumors in the breast do occur.

(2) Ten cases have been reported in the literature up to this writing.

(3) Two additional cases are here reported, one of renal origin, the other arising in a melanoma of the forearm.

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NEOPLASMS OF THE BONY THORACIC WALL

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TUMORS involving the thoracic wall and especially those arising from the ribs and sternum have been the subject of a number of scientific papers during the last 60 years. Because of the relative infrequency of primary neoplasms of the ribs and sternum, many reports of single cases with short periods of follow-up have appeared. The earlier writers were concerned with the dangers of open pneumothorax during operation, and Parham,⁶⁰ in his notable contribution divided the collected and his two personal cases, into groups with and without open pneumothorax at operation. With the present-day methods of administration of inhalation anesthetics with closed systems, and the use of positive pressure anesthesia, when necessary, or rhythmic pulmonary insufflation, open pneumothorax is no longer an operative danger.

The ribs and sternum are not common sites of primary tumors of bone. Among 57 osteogenic sarcomata reported by Campbell¹⁵ only one originated in a rib, while one osteogenic sarcoma out of 41 studied by Pfahler⁶² arose in a rib. Meyerding⁷⁷ discussed 100 cases of osteogenic sarcoma, three of which were of costal and three of sternal origin. Campbell¹⁴ reported one case of Ewing's sarcoma of a rib among 23 cases, and Desjardins, Meyerding, and Leddy²⁰ one of a rib among 42 proven instances of Ewing's sarcoma.

A number of efforts have been made to collect the available reported cases of tumors of the thoracic wall. In 1933, Hedblom³⁹ gathered 291 cases, including those reported by himself³⁷ in 1921, and added 22 additional personal cases. In reviewing the original reports of the collected tumors in his³⁹ paper of 1933, it was noted that histologic diagnoses had not been made on a number of the tumors, some of which had been treated by roentgenotherapy, without biopsy. In his earlier paper Hedblom³⁷ included a number of instances of tumors metastatic to the bony thoracic wall, and in both papers did not present, in detail, all his own cases, but gave only statistical data concerning the majority of them. It is not possible, moreover, in many of the earlier reports to evaluate the nature of the neoplasm described. The cases of Fort²⁵ and Gatewood,²⁶ for example, were reported as sarcomata but are now listed by the Bone Sarcoma Registry of the American College of Surgeons as instances of benign giant cell tumor (Samson and Haight⁶⁸). Such corrections of diagnoses, in the light of new knowledge, are unfortunately rarely available.

In spite of the difficulty of determining accurately the nature and number

of earlier reported cases of tumors of the bony thoracic wall, it seemed to be of value to collect the cases reported since Hedblom's³⁹ study of 1933* and to present them with 15 cases from the University of Michigan Hospital. The recent advances in the technic of thoracic operations, it was thought, should be reflected in improved clinical results. No tumor described in the literature without apparent adequate histologic study has been accepted. The case of Smith⁷⁰ is not included since two different diagnoses were made, and the chondroma reported by Jitsuiki⁴⁸ is omitted since the description was exceedingly brief. Cases may appear twice in the literature as in the reports of Alessandri¹ and Vitale.⁷⁷ Myeloma has not been considered. Batts⁴ has presented 40 cases of multiple myeloma from the University of Michigan Hospital, 68 per cent of them involving ribs.

Diagnosis—The important symptoms of neoplasms of the bony thoracic wall are tumor and pain. Severe pain is often associated with malignant tumors. Among the patients presented in this report, fever, weight loss, dyspnea, palpitation, mild supposed gastro-intestinal distress, and pleurisy occurred only rarely. Pleural effusion was present in only two patients, both of whom had Ewing's sarcoma.

The most important means of diagnosis of tumors of the ribs and sternum is the use of roentgenograms, the value of which, in certain cases, is increased by special positioning of the patient, fluoroscopy, and artificial pneumothorax. Jacobaeus and Key,⁴⁵ and Matson⁵⁴ have shown that inspection of the pleural cavity, after pneumothorax, with the thoracoscope may be useful in establishing the correct diagnosis and the extent of the thoracic wall lesions. Biopsy and histologic study of the removed tissue may be necessary for a correct diagnosis. Obviously, the history of the case and the physical findings are important diagnostic aids.

Differential diagnosis requires a consideration of various lesions of the thoracic wall, pleura, lung, and mediastinum, including aneurysm, osteomyelitis, gumma, cold abscess, encapsulated empyema, empyema necessitatis, bronchial carcinoma (which may directly involve the thoracic wall), echinococcus cyst, and mediastinal tumors.

Treatment—The data assembled for this report have given little evidence that radiologic therapy is of great value in the treatment of tumors of the thoracic wall. In two instances of benign giant cell tumor favorable results were obtained, Neil's (Samson and Haight⁶⁸) patient was apparently cured by the use of radium, and roentgenotherapy caused the regression of the tumor in Hilt's⁴² patient. A striking palliative result was obtained by roentgenotherapy in a case of Ewing's sarcoma reported by Bergstrand,^{6, 7} in this patient, very extensive pulmonary metastases disappeared after treatment on two occasions. Death occurred one year after the second period of therapy. Except for these three favorable instances there are no reports of successful radiation therapy for bony thoracic wall tumors since 1933.

* The Quarterly Cumulative Index Medicus was available to March, 1940—(Vol 27, No. 1)

Operative removal is the best means of therapy for tumors of the bony thoracic wall. The results of treatment by surgical means are dependent upon the nature of the tumors and the adequacy of their removal. The varying results of treatment of different types of tumors are discussed later in the article. All operations for tumors of the ribs and sternum should be carefully planned for adequate removal with resection of sufficient bony and soft parts. Attempts to excise tumors of the ribs and sternum extrapleurally, lead to partial removal with recurrence, the only too frequent result. The failure of improper resection of a tumor is well illustrated by Cabot Case No 24212¹³—four excisions of the tumor preceded the final operation for its removal, which was followed by the discovery of metastases in the lung. This tumor, which recurred four times before metastases became apparent, was considered benign at the time of the first four operations. With the employment of proper methods of anesthesia the thoracic cavity should always be opened at operation. Provision must be made for airtight closure of defects in the thoracic wall after removal of bony structures. Jones¹⁶ has described the replacement of the anterior portion of the second rib by use of part of the adjacent third rib as a pedicled graft, in this manner he assured the stability of the anterior thoracic wall following the removal of a tumor of the second rib.

Remarkably extensive resections of the sternum, with opening of both pleural cavities, have been successfully performed by Heuer¹¹ and John Alexander (Authors' Case 2). Haight (Authors' Case 9) also resected the *gladiolus sterni* and opened the left pleural cavity for chondrosarcoma. Nissen⁵⁷ removed a large osteogenic sarcoma with long lengths of four ribs anterolaterally, and a generous portion of the upper lobe of the lung infiltrated in continuity by the tumor, the patient recovered from the operation without especial difficulty. Hautefort³⁶ described the successful removal of a round cell sarcoma with the third, fourth, and fifth ribs and the middle lobe of the right lung from a four-year-old child, the tumor was adherent to, but had not infiltrated the lung.

Case 1 of this article exemplifies the treatment of a costal tumor by a properly planned operation. Following the admission of the patient to the University of Michigan Hospital, roentgenograms were made in oblique projections after the induction of artificial pneumothorax to obtain information in addition to that furnished by postero-anterior roentgenograms. These films demonstrated that the tumor, which was considered to be an osteogenic sarcoma, arose from the posterolateral portion of the left sixth rib and that it was not adherent to the lung. Fluoroscopic examination was also carried out. At operation a parascapular incision was carried well forward below the tip of the scapula, the trapezius and rhomboideus major and latissimus dorsi muscles were divided, and the scapula was retracted. The skin and muscles were divided at different levels in order to avoid overlying suture lines following closure of the wound. The tumor was not adherent to these muscles. The sixth rib was divided at the level of the vertebral transverse process and

the pleural cavity was opened posteriorly. A long length of the rib was removed with the adjoining intercostal muscles, which were divided close to the fifth and seventh ribs. Even though the approximation of the intercostal structures was not possible, airtight closure of the large wound was readily obtained by careful suture of the extracostal muscles, the subcutaneous tissues, and the skin, after reexpansion of the lung. Examination of the tumor demonstrated the absence of infiltration of the intercostal muscles—the histologic diagnosis was osteoma. Every care had been taken, however, to secure the complete removal of a tumor considered to be malignant before operation.

The treatment of metastatic tumors of the lung secondary to primary tumors of the ribs and sternum has been quite unsatisfactory, as might be expected, since the primary tumors themselves have been resistant to roentgenotherapy. The favorable result of treatment of one metastatic Ewing's sarcoma has been mentioned. Recently, Churchill¹³ has successfully removed the lower lobe of the right lung with an adjacent portion of the diaphragm for a metastatic osteogenic sarcoma, the primary site was in the left fourth rib. This represents the first reported operative treatment of an hematogenous metastatic pulmonary tumor with the primary focus in a rib.

For this article, a classification of tumors based upon histologic structure has been used. Zininger⁷⁸ proposed a clinical classification of neoplasms of the thoracic wall, dividing them into tumors arising from the deep structures of the thoracic wall and partially intrathoracic, those arising from the superficial structures but fixed to the deep structures, and those arising within the thorax and presenting through the thoracic wall. The primary interest of the present discussion is in the treatment of tumors involving the ribs and sternum. It is often difficult, clinically, to draw a sharp line between neoplasms arising primarily in the bony thoracic wall and those primary in the soft tissues involving the ribs and sternum secondarily. Probably none of the cases of fibrosarcoma, neurofibroma, schwannoma, lymphosarcoma, and Hodgkin's disease, to be presented, originated in any case in the bony thoracic wall in spite of their intimate association with it.

In order that a proper evaluation of the results of therapy of the different histologic types of tumors involving the ribs and sternum may be obtained, the collected cases, together with those from the University of Michigan Hospital, have been tabulated. The results of treatment vary strikingly in the benign and malignant groups. Unfortunately, long periods of follow-up are available for only a comparatively small percentage of the cases. In many instances reports were made shortly following successful operations. A comparison is available from these data of the operative mortality in treatment of benign and malignant tumors and to some extent of the late results of treatment.

OSTEOMA

Table I lists data concerning five cases of osteoma of the ribs, including one fibro-osteoma and one chondro-osteoma. There were four women and

one man, with ages varying from 24 to 49 years. Tumor and pain were the only symptoms, but they occurred together in only one case. The pain of the patient of Klapp⁵¹ was caused by pressure of a tumor of the first rib on the brachial plexus. In Case 1 of this report the pain was of a pleuritic type and was associated with a temperature of 101° F., pulmonary tuberculosis was suspected and roentgenographic study demonstrated the tumor, which could not be palpated. The duration of symptoms varied from one month to 30 years. All five tumors, the largest 25 cm. in diameter and the smallest 5 cm. in diameter, were successfully removed at operation. Follow-up data are available on only one patient, who is well two years after operation.

TABLE I
OSTEOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Result	Histo- logic Diagnosis	Remarks
(1) Jeannency and Chabot ¹⁷	F	19	11th rib	Bil- lateral ball	Pain	—	4 yrs	Removal, with 11th rib	Survived operation	Osteoma	Pain fol- lowed trauma
(2) Andrus	M	42	5th rib	25 cm in diam- eter	Tumor	—	30 yrs	Removal	Survived operation	Osteoma	Tumor followed fracture
(3) Klapp ⁵¹	F	28	1st rib anterio- rally	Duck egg	Tumor	Pain in brachial plexus distribu- tion	18 mos	Removal, with 1st rib	Survived operation	Fibro- osteoma	
(4) Gutierrez ²⁰	F	24	3rd rib antero- laterally	5 cm in diam- eter	Pain	Tumor	1 mo	Removal, with 3rd rib	Survived operation	Chondro- osteoma	
(5) Authors' (Case 1)	F	26	6th rib postero- laterally	8x5x5 cm	Pain	Temp 101° F	2 mos	Removal, with 6th rib	Well 2 yrs later	Osteoma	

Author's Case 1—M. B., white, female, age 25, was admitted July 20, 1938. For two months she had suffered with mild pleuritic pain beneath the left breast. One week previous to admission she had consulted a physician, who found her temperature to be 101° F. A tuberculin test was positive, and a roentgenogram revealed a tumor arising from a rib on the left. Physical examination disclosed a moderately obese white woman, with compensated rheumatic heart disease with mitral stenosis and insufficiency. There was no palpable evidence of a costal tumor. Roentgenograms (Figs. 1 and 2) demonstrated a well-localized, dense tumor with areas of translucency involving the axillary portion of the sixth rib. The tumor was thought to be an osteogenic sarcoma, with osteochondroma and osteoma as possibilities. A left pneumothorax was induced July 21, 1938. The tumor was removed July 23, 1938, according to the operative procedure described already. A satisfactory recovery from operation ensued, with air and fluid being aspirated on several occasions from the left pleural cavity. The patient was discharged two weeks after operation.

The tumor (Fig. 3) was described as an osteoplastic growth on the pleural surface of a rib, measuring 6x3x3 cm., with several cystic foci. Microscopic examination, after decalcification, showed dense bone with fatty marrow and some proliferating bone. *Pathologic Diagnosis*: Osteoma. The patient is well in July, 1940, two years following removal of the tumor.

CHONDROMA

In Table II are grouped 16 cases of chondroma of the ribs and sternum. Eleven occurred in men, four in women, and one in a three and one-half months'-old boy. The ages of 15 patients ranged from 21 to 55 years. In addition to the common symptoms of tumor and pain, dyspnea, mild digestive symptoms, and loss of weight each occurred once. One patient had no symptoms referable to the tumor, which was discovered by fluoroscopic examination.

FIG 1

FIG 2

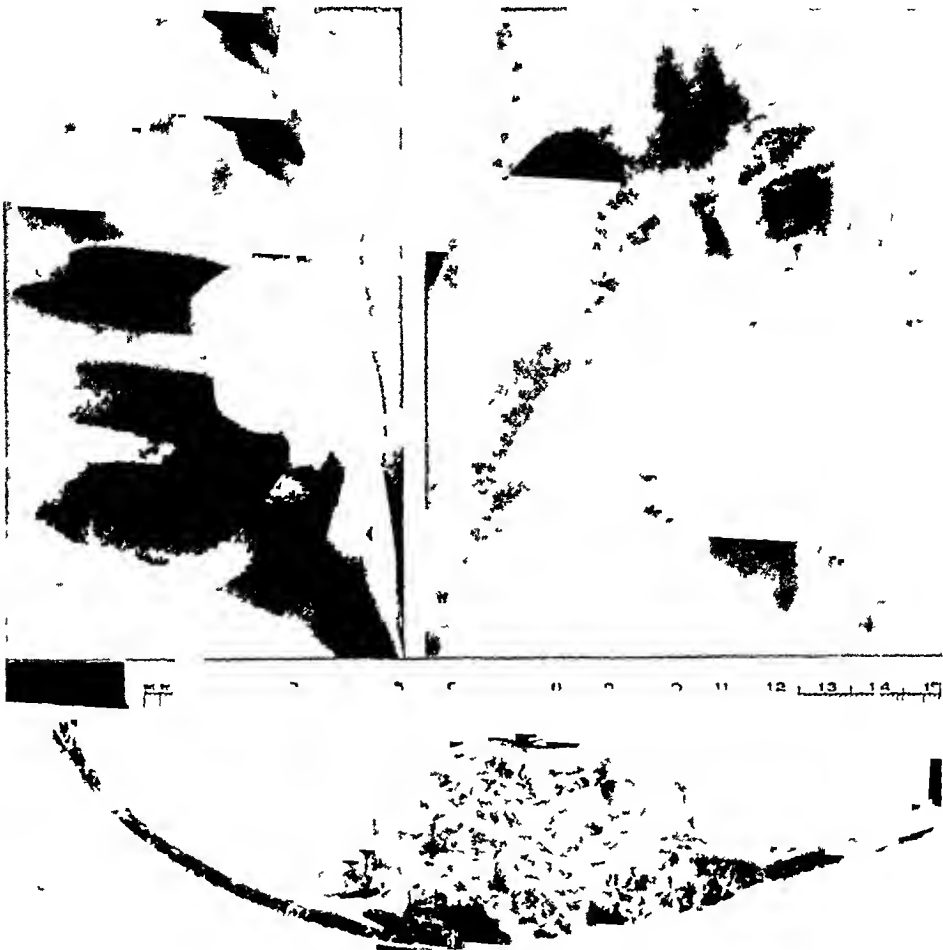


FIG 3

- FIG 1—Case 1 Postero-anterior roentgenogram of osteoma of left sixth rib
 FIG 2—Case 1 Lateral roentgenogram of osteoma of left sixth rib
 FIG 3—Case 1 Longitudinal section of osteoma of rib

tion during an industrial employees' health examination. With one exception, a tumor two centimeters in diameter, the chondromata were of moderate or large size. All 16 neoplasms were removed surgically, with one postoperative death following removal of a football-sized tumor. The operative mortality in this group was 6.2 per cent. Two resections were considered incomplete by the surgeons, the two patients are reported living and well, one and five years, respectively, following operation. Eight additional patients are living and well, eleven, seven and one-half, four, three and one-half, two, and one and two-thirds years, and six and five months, respectively, after operation.

Follow-up data after operative recovery are not available on five patients. In only one case was roentgenotherapy administered after operation.

The chondromata are often mentioned as tumors likely to become malignant after years of benign growth. Such a change may have occurred in the cases of Auchincloss,¹ whose tumor was of seven years' duration at the time of treatment, at autopsy a nodule of similar structure to the costal osteochondroma was found in a lung. The tumor of Golla's²⁹ patient was of 14 years' duration, without malignant change in spite of recurrence, while in the cases of Sokolov,⁷¹ Haipei,¹² and Santy⁶⁰ the tumors were of ten, six, and four years' duration, respectively before treatment.



FIG 4—Case 2, Lateral roentgenogram of recurrent chondroma of *gladiolus sterni*, the posterior projection of the tumor against the heart is shown.



FIG 5—Case 2, Oblique roentgenogram of recurrent chondroma of *gladiolus sterni*.

Author's Case 2—A O, white, male, age 34, was admitted January 1, 1932. About one year previously he had noted a dull ache over the lower portion of the sternum and shortly afterwards a small nodule appeared in this region, which was hard and which grew steadily. October 3, 1931, following a biopsy, a growth the size of a baseball was removed from the sternum, leaving only a thin shell of bone posteriorly, from which tumor tissue was curetted. The neoplasm promptly recurred and grew rapidly. On examination the patient presented a mass over the sternum from the level of the second rib to the fourth interspace, measuring 5.3x4.1 inches. The tumor was irregular with rounded nodules, it was rubbery at the upper pole, but hard and fixed inferiorly. To the right of the midsternal line was a four-inch vertical scar centered at the level of the third interspace. Roentgenographic examination (Figs 4 and 5) showed a tumor involving the middle third of the sternum, projecting posteriorly against the heart as well as anteriorly, there was irregularity in the density of calcification in the tumor. A diagnosis of osteochondroma was made. A biopsy specimen showed a cellular chondroma.

Operation—January 13, 1932. An incision from the suprasternal notch to the xiphoid was made with excision of the soft tissue over the tumor. The right third and fourth cartilage were resected to afford access to the mediastinum. The tumor, which was adherent to the right pleura, was dissected free from the pericardium and other mediastinal structures after division of the cartilages from the third to seventh, bilaterally. Both

TABLE II

CHONDROMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Result	Histologic Diagnosis	Remarks
(1) Sorrel and Oberthur ⁷²	M	11	2nd rib anteriorly	Large	Tumor	—	—	Partial removal	Well 1 yr later	Chondroma	Tumor adherent to great vessels and pericardium
(2) Potvin ⁶⁴	M	26	10th rib anteriorly	Child's head	Mild digestive symptoms	Tumor, loss of weight	3 mos	Removal with 10th rib	Survived operation	Chondroma	
(3) Follhasson and Blanchard ⁷³	M	3½ mos	6th rib at angle	5½x5 cm	Tumor	—	1 mo	Removal, with 6th and 7th ribs	Survived operation	Chondroma	
(4) Auchincloss ³	M	23	7th to 10th rib anterolaterally	Football	Tumor	Pain and dyspnea	7 yrs	Removal with two stage operation	Postoperative death	Osteochondroma	Similar nodule found in lung at autopsy, metastatic lesion?
(5) Sokolov ⁷¹	F	37	8th to 10th ribs and cartilages	Fist	Tumor	Pain	10 yrs	Removal with 8th to 10th ribs	Discharged from hospital well	Chondroma	
(6) Moura and Rodrigues ⁶⁶	M	21	1st rib posteriorly	Orange	Tumor	—	4 mos	Removal with 1st rib followed by x ray therapy	Well 2 yrs later	Osteochondroma	Presented in neck
(7) Santves ⁶⁸	M	38	3rd and 4th ribs anteriorly	Orange	Tumor	Pain	4 yrs	Removal with 3rd and 4th ribs	Survived operation	Chondroma	
(8) Golia ⁷⁰	F	55	3rd and 4th ribs anteriorly	Child's head	Tumor	Pain	9 yrs	Previous incomplete removal, with 3rd-4th used to grow ribs, extensive operation to remove recurrent tumor 5 yrs later	Recurred in 2 yrs and continued to grow Well 5 mos after 2nd operation	Chondroma	14 yrs total duration

NEOPLASMS OF THORACIC WALL

(9) Harper ²¹	F	17	4th rib and cartilage	5x1 cm	Tumor	—	1 yr	Removal with 4th rib and cartilage	Well 6 mos later	Chondroma	
(10) Harper ²²	M	41	6th rib anteriorly	10x3x3 cm	Pain	—	6 yrs	Removal	Well 3 1/2 yrs later	Probably chondroma	Pain referred to upper abdomen. Had been treated for gallbladder disease. Diagnosis made during industrial chest survey.
(11) Jones ¹⁶	M	30	3rd rib and cartilage	7x5 cm	—	—	—	Removal with rib and cartilage	Survived operation	Chondroma	
(12) Jones ¹⁶	M	40	9th rib antero-laterally	Orange	Pain	Tumor	2 yrs	Removal, with 9th rib and cartilage	Well 11 yrs later	Osteochondroma	
(13) Authors' Case 2	M	34	Gladiolus sterni	12x6x6 cm	Pain	Tumor	1 yr	Previous partial removal, resection with gladiolus sterni	Well 7 1/2 yrs later	Chondroma	Both pleural cavities opened during operation. Recurrence in costal cartilage, widely removed.
(14) Authors' Case 3	M	47	7th rib at head and neck	Orange	Pain	Tumor	3 mos	Incomplete removal with 6th to 9th ribs	Well 5 yrs later	Chondroma	
(15) Authors' Case 4	M	26	Gladiolus sterni at junction with manubrium	2x2x2 cm	Tumor	Pain	6 mos	Removal	Well 1 yrs later	Chondroma	Exceptionally early case
(16) Authors' Case 5	F	55	10th rib	9 1/2x8 cm	Tumor	Pain	1 yr	Removal, with 9th, 10th, 11th ribs	Well 20 mos later	Osteochondroma	

pleural cavities were entered, and the pleural openings were later closed with catgut sutures. The sternum was divided just below the manubrium and above the xiphoid. The pectoralis major muscles, which had been mobilized, were sutured together and the skin closed without drainage.

Following operation the right lung was collapsed about 50 per cent and the left only slightly. Fluid developed in the right pleural cavity, which became purulent and was drained, with rib resection, February 16, 1932. Wound infection occurred and involved the seventh and eighth cartilages, which were resected in part with some of the xiphoid May 9, 1932. The patient was discharged May 13, 1932, with the empyema and operative wounds draining.

The tumor, which is illustrated in longitudinal section (Fig 6), was again shown, histologically, to be a chondroma. The patient returned August 13, 1932, with a tumor

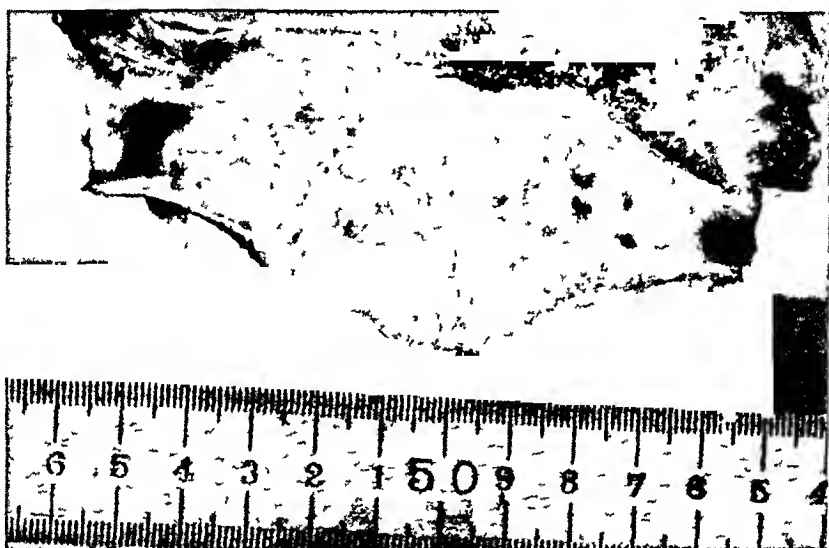


FIG 6—Case 2 Longitudinal section of recurrent chondroma of *gladiolus sterni*, with attached soft parts

mass at the lower end of the sternum and a persisting sinus track at the lower end of the wound. August 27, 1932, the wound was explored, with removal of a cystic mass, apparently cartilage, one centimeter in diameter. On pathologic examination, several small islands of atypical, presumably neoplastic cartilage, constituting a recurrence, were found, there was no evidence of sarcomatous change.

After the second discharge of the patient a plastic operation was successfully performed elsewhere, in order to close the persisting right empyema with bronchopleural fistula. June 20, 1939, seven and one-half years after operation, the patient reported that he was quite well and doing full-time work.

Author's Case 3—J. R., white, male, age 47, was admitted, February 8, 1934, complaining of pain in the posterior left thorax of three months' duration, and of a tumor mass of three weeks' duration. Examination revealed a bony hard, fixed tumor the size of a small orange just to the left of the seventh dorsal spine. Roentgenographic examination (Fig 7) demonstrated a somewhat cystic tumor arising from the head, neck, and the tubercle of the left seventh rib with pressure deformity of the adjacent ribs and of the sixth and seventh dorsal vertebrae, there were thinning and bulging of the cortex of the seventh rib. The diagnoses considered were giant cell tumor, hemangioma, osteochondroma, and osteogenic sarcoma. A biopsy specimen, taken February 10, 1934, showed it to be a chondroma. The tumor was removed February 14, 1934, by resection of the sixth to the ninth ribs posteriorly. Although the parietal pleura was readily stripped from the tumor, several tears were made in it. A part of the tumor had ap-

TABLE III
MALIGNANT CELL TUMOR

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Dura- tion	Treatment	Result	Histologic Diagnosis	Remarks
(1) Fort	M	11	1st rib and clavicle	—	1 tumor	—	8 mos	Excision with por- tions of clavicle 1st rib and sternum (had previous op- eration)	Well 17 yrs	Benign giant cell tumor	Originally re- ported as sarcoma
(2) Gatewood	F	14	12th rib	5x3x3 cm	Pain	1 tumor	1 yr	Excision, radium	Well 13 yrs	Benign giant cell tumor	Originally re- ported as sarcoma
(3) Purcell	M	17	10th rib	Large	1 tumor	Myelitis	9 mos	X-ray, excision with 6th to 12th ribs	Postoperative death	Chondroma osteo- genic sarcoma aris- ing in benign giant cell tumor	History of trauma
(4) Hedblom	F	36	6th rib posteriorly	—	Pain	—	3 yrs	Intercostal neuroec- tomy for pain, re- section later	Well 11 yrs	Benign giant cell tumor	
(5) Holland	M	46	5th costochondral junction	1x3x3 cm	1 tumor	—	6 mos	Excision	Well 11 yrs	Benign giant cell tumor	
(6) Neil (Sanson and Hight)	M	9	11th rib at angle	Small	Pain	1 tumor	2 mos	Biopsy and radium	Well 11 yrs	Benign giant cell tumor	
(7) Sanson and Hight	F	31	2nd costochondral junction	3.5x2x2 cm	1 tumor	—	2 yrs	Removal	Well 5.3 yrs	Benign giant cell tumor	
(8) Hight	F	15	5th rib at angle	3.5x3x3 cm	1 tumor,	—	6 mos	Biopsy and x-ray	1 yr and 10 mos later tu- mor smaller and calcified	Benign giant cell tumor	History of trauma
(9) Jones	M	19	7th rib postero- laterally	8x5 cm	Pain	—	10 mos	Removed	Died 2 1/2 yrs later of bron- chial carcinoma	Benign giant cell tumor	

parently invaded the vertebral bodies, and this part was not removed. The wound was closed without drainage after expansion of the lung. Convalescence was complicated by a sanguineous left pleural effusion that became purulent. Intercostal drainage was followed by open drainage, with rib resection. The patient was discharged June 8, 1934, with a narrow, draining track, which later healed.



FIG 7—Case 3. Posteroanterior roentgenogram of chondroma of posterior end of seventh left rib.



FIG 8—Case 4. Lateral roentgenogram of a very early chondroma at joint between manubrium and *gladiolus sterni*.

Pathologic examination confirmed the earlier diagnosis of chondroma growing in cancellous bone. The patient reported himself quite well, March 27, 1939, five years after operation.

Author's Case 4—C V, white, male, age 26, entered the hospital, November 27, 1934, complaining of a lump over the upper sternum, which had slowly increased in size since its appearance six months previously. Four months before admission, pain on pressure over the tumor had become noticeable and for three months cough and expectoration of thick sputum, tinged with blood, had been present. Twenty-six pounds had been lost during the previous two years. Examination disclosed a red, tender, firm swelling over the sternum, three centimeters below the suprasternal notch. Roentgenograms (Fig 8) showed an irregular moth-eaten appearance of the joint between the manubrium and *gladiolus sterni* with some tumefaction external to the anterior sternal surface; sclerosis of the surrounding bone was present. There was evidence in the films of inactive, minimal, right apical pulmonary tuberculosis. November 28, 1934, the tumor was exposed and found to project seven millimeters anterior to the joint between the manubrium and gladiolus and to reach two centimeters above and below the joint. The tumor, together with the joint, was removed. No pus or other evidence of inflammation was found. Bone was removed to a depth of one centimeter from the anterior sternal surface—entirely removing the neoplastic tissue, and the wound was closed in layers, without drainage.

Histologically, the decalcified tissue of the tumor showed atypical new formation of cartilage in small nodular masses replacing bone, no defensive exudation inflammation was present, but there was new formation of connective tissue in the marrow spaces. The diagnosis was chondroma or osteochondroma, which was not sufficiently cellular to be regarded as sarcomatous. Roentgenographic study, November 15, 1935, one year

later, showed complete filling-in of the operative defect. When seen April 6, 1937, the patient presented no evidence of tumor. January 6, 1939, four years after operation, he had no signs or symptoms referable to the sternal chondroma.

Author's Case 5—M. B., white, female, age 55, was admitted, November 3, 1937, complaining of a lump over the lower left ribs for the past year with some pain and tenderness. The mass had grown slowly for seven months before admission. Four years previously she had suffered possible fractures of the ribs in the region of the lump. A stony hard, fixed mass, was palpable in the left midaxillary line and was attached to the tenth rib. All borders were well defined except the inferior, which seemed to reach almost to the crest of the ilium. A pyelogram showed a normal position of the left kidney and roentgenograms of the thoracic wall, a somewhat loculated tumor arising from the left tenth rib in the midaxillary line without apparent invasion of adjacent ribs. The diagnosis of giant cell tumor with probable malignant change was made, osteochondroma and chondrosarcoma were also considered. The tumor was removed November 9, 1937. A diagnosis of myxochondroma was made from frozen-section examination of a portion of the tumor. The ninth, tenth, and eleventh ribs were divided at the level of the lateral border of the sacrospinalis muscle. The tumor was removed *en masse* after opening of the pleura. The peritoneum was dissected from the tumor. The patient was discharged two weeks later.

The tumor measured 10x8x8 cm, it was surrounded by fat, and three ribs extended into it. Paraffin sections demonstrated more bone formation than had the frozen sections. A diagnosis of osteochondroma, which was somewhat invasive where it made contact with muscle, was made. The patient was reported as well, without recurrence, by her family physician, July 7, 1939, 20 months after operation.

BENIGN GIANT CELL TUMOR

Because of the rarity of benign giant cell tumor of the ribs, it seemed of interest to review all the cases adequately described in the literature. In 1935, Samson and Haight⁶⁸ presented an example from the University of Michigan Hospital. Additional follow-up information is available on this patient and is given in Table III, with data regarding six other patients from the paper of Samson and Haight, and two reported since 1935. Three cases included by Samson and Haight have been omitted because of unsatisfactory reports. Among the group listed are the instances reported originally by Fort,²⁵ and Gatewood²⁶ as sarcomata, the diagnoses having been changed by the Bone Sarcoma Registry of the American College of Surgeons to benign giant cell tumor.

Five of the benign giant cell tumors listed in Table III occurred in men, and four in women. The ages ranged from nine to 49 years. Tumor and pain were the only symptoms except for weight loss in one case with malignant change. The symptoms were of two months' to two years' duration. Two patients were treated only with radium and roentgenotherapy, respectively, with apparently good results, and are reported as living 11 years, and one year and ten months, respectively, following treatment. The remaining seven patients were treated by operative removal of the tumors with one postoperative death occurring following the removal of a chondro-osteogenic sarcoma arising in a benign giant cell tumor. A second patient died of bronchial carcinoma two and one-half years after successful removal of the benign giant cell tumor. The remaining five patients all represent "five-year cures" by

suigical treatment, and are reported living and well from 17 to five and one-third years after operation, one patient had radium therapy after removal of the tumor

The case of Samson and Haight⁶⁸ is listed as *ostetis fibrosa cystica* by the Bone Sarcoma Registry of the American College of Surgeons. No reference to this disease affecting the ribs or sternum has been found in the literature

OSTEOGENIC SARCOMA

Table IV lists 18 cases of osteogenic sarcoma of the ribs and two of the sternum, 14 occurring in men and six in women. The ages varied from 12 to 66 years. Aside from the symptoms of pain and tumor, pathologic fracture, palpitation and dyspnea, each occurred one time. The symptoms varied in duration from one week to eight years. One patient was not treated because of the presence of metastases to the regional lymph nodes and extensive local infiltration of the tumor. The neoplasms of 19 patients were removed at operation, with one postoperative death of a patient whose tumor was extensively adherent to the lung and diaphragm. Roentgenotherapy was administered in three instances following operation, once in conjunction with Coley's toxins. One patient received preoperative roentgenotherapy and Coley's toxins after the incomplete removal of an extensive chondrosarcoma. Six patients are reported dead, one postoperatively and one without treatment, one lived 11 years after the initial symptoms, before dying of his disease, six years after a second operation. Five patients are reported living with recurrent and metastatic lesions, and one additional patient, recently, has had a resection of the lower lobe of the right lung for an hematogenous metastatic tumor. Six patients are living without disease from two months to three years after treatment. Follow-up information, other than of operative recovery, is not available on two patients. No five-year cures are reported.

Some evidence bearing upon the occurrence of malignant change in benign costal neoplasms is afforded by Cabot Case No. 24212,¹³ in which a costal tumor was removed four times before a metastatic pulmonary lesion became apparent. The untreated Case 8 of this article died of a massive tumor of eight years' duration, the growth of which had been slow until shortly before death, metastases to regional lymph nodes were present.

Author's Case 6—J. B., white, male, age 34, entered the hospital December 6, 1932. Eight months previously he had fallen ten feet, striking the right side of his back and fracturing several ribs. Three months before admission he had noted a lump on the right side of the chest, accompanied by severe pain, the tumor and pain had persisted. An orange-sized mass was palpable at the level of the eighth to tenth right ribs lateral to the spine. Pathologic examination of gelatinous material aspirated from the tumor demonstrated it to be a chondrosarcoma but not sufficiently cellular to make metastasis likely. Roentgenograms showed an increase in the soft tissue shadow of the right thoracic region due to the tumor, with erosion of the eighth and ninth right transverse vertebral processes and of the vertebral portion of the right tenth rib. A number of discrete calcified lesions of the lungs were thought to be of tuberculous origin. Roentgenotherapy, with a

total dosage of 1,600 roentgen units was administered, and the patient was discharged. He was readmitted and, January 13, 1933, the tumor was found at operation to have infiltrated the sacrospinalis muscle and to have invaded the thorax to an extent that made complete removal impossible. Coley's toxins were given after this operation without benefit. He again returned to the hospital suffering with severe pain and a complete transverse myelitis, which was not relieved by laminectomy. He died September 12, 1933. Postmortem examination disclosed extensive pulmonary and epidural metastases in the region of the dorsal cord with one intradural tumor mass.



FIG 9—Case 7 Postero anterior roentgenogram of chondrosarcoma of right sixth rib

Author's Case 7—V W, white, female, age 24, was admitted November 30, 1937. In June, 1937, she had noted for two days sharp pain in the right axillary region and beneath the right breast, which had been aggravated by deep inspiration and movement of the right arm. During July, 1937, stiffness of the right arm was present, with cough and expectoration of foul yellow sputum. For three weeks prior to admission the patient had been aware of a swelling in the right axillary region, with a sensation of heaviness of the arm. On examination, there was felt a fixed tumor mass beneath the right posterior axillary fold, two small nodes were palpable in the right axilla and one in the left, and there was some fulness of the right supraclavicular region. Roentgenologic examination (Fig 9) demonstrated a tumor arising from the axillary portion of the sixth rib, with irregularity in its architecture and elevation of the periosteum, secondary pressure deformity of the seventh rib was present, and the tumor extended into the chest. A diagnosis of Ewing's sarcoma was considered most likely, although osteogenic sarcoma

TABLE IV
OSTEOGENIC SARCOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis	Remarks
(1) Vannoy ⁷⁶	M	29	8th, 9th and 10th ribs laterally	Nut	Tumor	—	4 yrs	Removal with 8th to 10th ribs	Well 3 yrs later	Chondrosarcoma	History of trauma
(2) Biggers ³	F	12	7th rib	—	Pathologic fracture	—	—	Removal	Survived operation	Osteogenic myofibrosarcoma	
(3) Butler ¹⁰	M	44	10th rib	—	Pain	Tumor	1 wk	Removal	Well 3 yrs later	Osteogenic sarcoma	
(4) Cabot Case No 192021 ¹⁰	M	42	Several ribs (adherent to lungs and diaphragm)	Very large	Tumor	—	3½ yrs	Partial removal	Postoperative death	Osteogenic sarcoma (chondrosarcoma)	
(5) Matson ⁴	F	27	7th rib (adherent to lung)	10x7x6 cm	Pain	Tumor	9 mos	Removal with 3 ribs and portion of lung, x-ray, Coley's toxins	Well 1½ yrs later	Osteogenic sarcoma	
(6) Papin ¹⁸	F	43	3rd, 4th, 5th ribs anteriorly	15 cm diam	Pain	Tumor	—	Removal with 3rd to 5th ribs	Well 14 mos later	Chondromyxosarcoma	Largely intrathoracic
(7) Campbell ¹⁵	M	38	Several ribs	Large	—	Tumor pain	2 yrs	Partial removal	Died of metastases 3 yrs later	Chondrosarcoma	
(8) Didier ¹	F	38	Costal cartilages	14x12 cm	Tumor	—	2 yrs	Removal, x ray	Recurred 6 mos later	Chondroosteosarcoma	Multiple cartilaginous exostoses on bones
(9) Halpert and Davis ³¹	M	41	12th rib	—	—	—	—	Removal	Recurred 8 mos later with epidual and pulmonary metastases	Chondrosarcoma	
(10) Nissen ⁷	M	32	2nd to 5th rib anteriorly	20x15x15 cm	Tumor	Dyspnea palpitation	1 yr	Removal with 4 ribs and portion of lung	Survived operation	Osteosarcoma	Extensive operation
(11) Roberg ⁶⁸	F	39	Manubrium and <i>gladiolus sterni</i>	Goose egg	Pain	Tumor	1 yr	Removal with division of 2nd to 5th cartilages, removal of remaining portion of manubrium 6 mos later, x ray after each operation	Recurred with pulmonary metastases 11 mos after second operation	Chondroma with partial transition to sarcoma	

NEOPLASMS OF THORACIC WALL

(12) Speed ¹	M	62	2nd 3rd 4th ribs anteriorly	23x16x10 cm	Tumor	—	3 yrs	Removal with 2nd 3rd and 4th ribs and cartilages	Recurred in 6 mos	Chondrosarcoma	Total duration 11 yrs
(13) Speed ¹³	M	40	2nd 3rd 4th ribs anteriorly	20x16x10 cm	Tumor	Pain	5 yrs	Previous removal, removal with 3 ribs portion of sternum and pericardium	Died of persistent local growth and metastases, 6 yrs later	Chondrosarcoma	
(14) Cabot Case No 24212 ¹³	M	28	Left 4th rib posteriorly	Small	Tumor	—	5½ yrs	Removal of recurrent tumor (4 previous operations in 5-yr period)	7 mos later metastatic tumor in rt lower lobe of lung	Osteogenic sarcoma	Apparently benign chondroma Successful removal of rt lower lobe and portion of diaphragm for metastatic tumor
(15) Jones ¹⁶	M	54	11th rib	Large	Tumor	—	1 wk	Removal with 10th and 11th ribs	Well 1 yr later	Osteogenic sarcoma	
(16) Jones ¹⁶	M	63	3rd rib and cartilage	7x6x5 cm	Tumor	—	1 mo	Removal	Extensive local recurrence 1 yr later	Chondrosarcoma	
(17) Authors' Case 6	M	34	8th 9th 10th ribs posteriorly	Orange	Tumor Pain	—	8 mos	X-ray, partial removal, Coley's toxins	Died 7 mos after operation of persistent tumor and metastases to spine and lungs	Chondrosarcoma	
(18) Authors' Case 7	F	23	5th 6th ribs laterally	—	Pain	—	6 mos	Removal with 5th, 6th 7th ribs	Metastases to spine occurred 9 mos later, died 25 mos postoperatively of multiple metastases	Chondrosarcoma	X-ray therapy given after biopsy of metastatic lesion with improvement
(19) Authors' Case 8	M	66	Ribs of intercostular region	Large	Tumor	Pain	8 yrs	Partial excision elsewhere, biopsy of metastatic lesion	Died 2 mos later	Myochoondroma	Bilateral pulmonary and local metastases present
(20) Authors' Case 9	M	49	Gladiolus sterni	12x6x6 cm	Tumor	—	5 mos	Removal with gladiolus sterni	Well, 2 mos later	Chondrosarcoma	

was thought possible. A biopsy specimen of the tumor was reported as a probable sclerosing carcinoma, with scattered spherical and polyhedral cells of epithelial type. Two lymph nodes, which histologic examination showed were normal, were removed from the right supraclavicular fossa. A right pneumothorax was induced, and attachment of the lung to the tumor was seen roentgenologically. December 17, 1937, the lobulated tumor protruding between the sixth and seventh ribs was exposed. The thoracic cavity

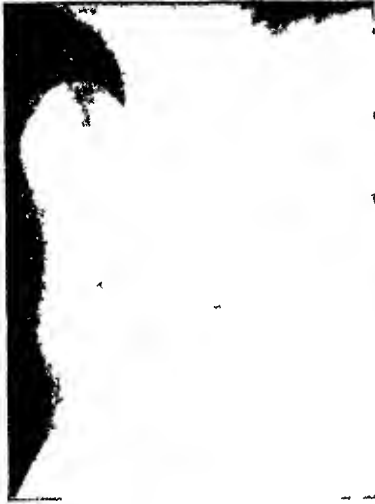


FIG 10—Case 9 Chondrosarcoma of gladiolus sterni

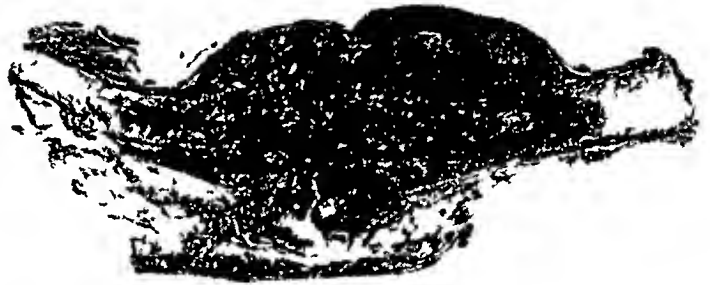


FIG 11—Case 9 Longitudinal section of chondrosarcoma of gladiolus sterni (Cf 7)

was opened through the bed of the resected fifth rib, well above the tumor, which was removed with segments of the sixth and seventh ribs, which were divided far anterior and posterior to the neoplasm, after ligation and division of the intercostal vessels. Sharp dissection was used to free the tumor from the lung. The patient made a satisfactory recovery, and was discharged January 9, 1938.

On cross-section, the tumor was seen to be composed of a soft tissue mass, six centimeters in diameter, surrounding a rib, from which spicules of bone radiated. Microscopically, the tumor was a malignant neoplasm made up of spindle cells around foci of atypical cartilage, part of the neoplasm, a chondrosarcoma, showed hyaline fibrosis, other foci were highly cellular with hyperchromatic nuclei. The opinion was expressed that local recurrence, rather than distant metastases, was to be feared. The patient returned August 13, 1938, with a swelling at the level of the fourth dorsal spine and mild pain radiating to the right scapular region. By December 12, 1938, this mass had increased in size and a biopsy specimen showed the same histologic structure as that of the tumor originally removed. Roentgenotherapy caused complete regression of the palpable tumor. In June, 1939, a metastatic lesion in the right lung was found and treated by roentgenotherapy. Further roentgenotherapy was administered because of pain in the shoulder region. In October, 1939, the patient became paralyzed, following collapse of the first dorsal vertebra. Death from multiple widespread metastases occurred January 25, 1940, 25 months after operation.

Author's Case 8—K. Z., white, male, age 66, was admitted December 17, 1938. He had noticed a small lump in the midline of the back eight years previously. Slow growth had taken place, until a rapid increase in size began in the Spring of 1938. The tumor was excised in September, 1938, but rapidly recurred, with an accompanying lump in the left axilla. Examination showed an irregular, firm mass five inches in diameter, fixed to the deep structures and lying across the midline, from the fourth to the tenth dorsal vertebrae. A scar, six inches long, lay across the tumor, above which was a firm, freely

movable nodule one inch in diameter. A golf-ball-sized mass was present in the left axilla and a smaller one in the right axilla. Roentgenographic examination of the thorax, in the lateral projection, demonstrated an ill-defined conglomerate mass of punctate density in the soft tissue of the posterior thoracic wall, which was thought to represent probable calcification in the tumor. The left axillary mass was removed and found, histologically, to be a myxochondroma adjacent to, and invading, a large lymph node, with wide infiltration of surrounding fat. The tumor was described as highly cellular and a recurrence with sarcomatous changes was predicted. The patient was discharged January 4, 1939, and died February 5, 1939.

Author's Case 9—E. C., white, male, age 49, entered the hospital February 28, 1940. For five months he had noticed a progressively growing nodule located over the center of the sternum. Slight cough and ease of fatigue had been present for one month. A portion of the mass had been removed one week previously and a diagnosis of chondrosarcoma made by histologic study. Over the midportion of the sternum (Fig 10) a firm, slightly tender mass was palpable, which was four centimeters in diameter and was elevated one centimeter above the surrounding tissue. A healing surgical scar lay over the tumor. Roentgenographic examination showed a destructive lesion involving the middle and lower portions of the sternum. Review of the pathologic sections confirmed the diagnosis of chondrosarcoma, which was more likely to recur locally after incomplete excision than to give rise to distant metastases. The patient was discharged to return after complete healing of the biopsy incision. The patient was readmitted, and, March 18, 1940, the tumor and sternum were removed. The third to the seventh left and the right costal cartilages were divided lateral to the tumor and the sternum was transected just below the manubrium. The tumor was carefully freed by blunt dissection from the pleurae and from the prepericardial fat. A small tear in the left pleura was left open to provide for drainage of wound serum into the left pleural cavity, so as to avoid cardiac tamponade. The wound was closed by mobilization and suturing together of the pectoralis major muscles in the midline, and by closure of the skin without external drainage. On the second day following operation intratracheal and intrabronchial catheter suction was employed to remove bronchial secretions. Further convalescence was uneventful. The patient was discharged April 20, 1940.

Pathologic examination of the tumor (Fig 11) again confirmed the diagnosis of chondrosarcoma. A marked similarity of the specimen to that of Case 2 (Fig 7) was noted. The roentgenographic appearance of the two neoplasms was also quite similar. The patient was well, May 21, 1940, two months after operation.

EWING'S SARCOMA

Table V lists data regarding 18 patients suffering with Ewing's sarcoma, apparently primary in ribs. In an effort to list all available cases of Ewing's sarcoma, primary in the bony thoracic wall, in the literature, the cases of Hedblom,^{38, 39} and Harrington,³⁴ reported as sarcoma and endothelioma, respectively, have been included since, from the published descriptions, the tumors were in all likelihood examples of this neoplasm. In addition, the case of Reeves and Kassabach,⁶⁵ included by Hedblom,³⁹ and two of Geschickter and Copeland,²⁷ omitted by Hedblom,³⁹ have been listed. In reviewing the cases collected by Hedblom,³⁹ five probable instances of Ewing's sarcoma were found in the reports of Key,⁵⁰ Juge, de Veinejoul, and Astier,⁴⁹ Denk,¹⁹ Polloson and Novel,⁶³ and Harrington,³⁴ these cases are not listed in Table V, since the evidence is not positive that they represented Ewing's sarcoma.

TABLE V
EWING'S SARCOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis	Remarks
(1) Hedblom ³³	M	15	4th rib anteriorly and laterally	12x6x4 cm	Pain	Tumor	9 mos	Removal with 3rd 4th 5th ribs, x-ray	Died 5 mos later of recurrence	Sarcoma	Photomicrograph and course typical of Ewing's sarcoma
(2) Harrington ³³	F	15	4th to 8th ribs posteriorly	Large	Pain	Tumor	5 mos	Partial removal with 4th to 8th ribs, radium	Death 3 mos later of pulmonary and spinal metastases	Endothelioma	
(3) Reeves and Kassabach ³⁵	F	18	9th rib posteriorly	8x5x5 cm	Pain	Pleurisy	3 mos	Partial removal with 8th 9th 10th ribs, x-ray, Coley's toxins	Death 10 mos after operation with metastases to lung pleura and liver	Sarcoma probably Ewing's	
(4) Geschickter and Copeland ⁷	F	15	4th rib	—	—	Tumor, pain	18 mos	Removal, second removal 18 mos later	Died few mos later	Ewing's sarcoma	
(5) Geschickter and Copeland ²⁷	M	27	Ribs	—	Dyspnea	Tumor	3 mos	Radiation	Died	Ewing's sarcoma	
(6) Tavernier ⁷⁸	M	12	11th 12th ribs 11th and 12th thoracic 1st lumbar vertebrae	Large	Pain	Tumor and paraplegia	6 mos	Biopsy and x-ray	Tumor not palpable but paralysis continued, died 6 mos later	Ewing's sarcoma	
(7) Campbell ¹¹	F	10	Rib	—	—	—	4 mos	X-ray	Well 2 mos later	Ewing's sarcoma	
(8) Dagneau Pichette and Morin ¹⁸	M	16	11th rib	10x6 cm	Tumor	Pain	3 mos	Removal with 11th and 12th ribs, x-ray (had two previous operations)	Recurrence and metastasis to lungs and skull, death after treatment of metastases	Ewing's sarcoma	Earliest diagnosis of infection
(9) Herbert ⁴⁰	M	10	6th rib laterally	—	Pain	Fever, pleural effusion	3 mos	Removal, x-ray	Died 1 mo later	Ewing's sarcoma	

(10) Herbert ¹⁰	M	20	3rd rib laterally	Large	Pain and tumor	Loss of weight	3 mos	Biopsy, x ray	Died very shortly	Ewing's sarcoma	Intrathoracic extension and pulmonary metastases present at time of diagnosis
(11) Bergstrand ^{6, 7}	M	15	5th and 6th ribs, posterolaterally	500 Gm	Pain	Tumor	15 days	Removal, x ray for metastases later	Pulmonary metastases 2½ and 5 yrs later which regressed with treatment, died of metastases 6 yrs after operation	Ewing's sarcoma	Excellent response to first roentgenotherapy
(12) Bergstrand ⁶	M	10	6th, 7th ribs, laterally	—	Malaise	Tumor, pain	6 mos	Removal, probably incomplete	Living, 1½ yrs later, with pulmonary and osseous metastases	Ewing's sarcoma	
(13) Bergstrand ⁶	M	10	6th, 7th ribs laterally	8x5 cm	Tumor	Pain	1 mo	X-ray, removal, with 6th and 7th ribs	Survived operation	Ewing's sarcoma	
(14) Bergstrand ⁶	M	14	8th rib, posteriorly	Right thorax filled	Pain	Tumor and dyspnea	12 mos	X-ray	Immediate improvement	Ewing's sarcoma	
(15) Geschickter and Copeland ⁸	M	22	Rib	—	Pain	—	12 mos	Curettage	Died 3 yrs later	Ewing's sarcoma	
(16) Geschickter and Copeland ⁸	M	30	Rib	—	Cough, pleurisy	—	6 mos	X-ray	Died 2 yrs later	Ewing's sarcoma	
(17) Geschickter and Copeland ⁸	M	11	Rib	—	Pain	Pleural effusion	3 mos	X-ray	Died 3 mos later	Ewing's sarcoma	History of trauma
(18) Authors' Case 10	F	22	11th rib posteriorly	9x8x6 cm	Pain	Tumor	2 mos	Biopsy, x-ray	Died 7 mos later	Ewing's sarcoma	8 mos pregnant at onset, uneventful delivery

The symptoms of the listed cases of Ewing's sarcoma of the ribs are tumor and pain with the addition of dyspnea, pleurisy, and pleural effusion, each two times, and fever, malaise, loss of weight, cough and paraplegia from metastases, each once. Thirteen patients were men, and five were women, whose ages varied from 10 to 30 years. In no case had symptoms been present for more than one year before treatment. The tumors were treated by operation alone in four instances, and by operation combined with irradiation in six instances, Coley's toxins were administered to one of the latter group of patients. Irradiation alone was the treatment administered to eight patients. There were no deaths due to operation.

The results of treatment of Ewing's sarcoma of the ribs were poor. Fourteen of the 18 patients are reported dead of their disease, ten dying 13, or fewer months after treatment, and three, two, three, and six years, respectively, after treatment. The duration of life before death of one patient is not stated. One patient is reported living with disease and one-half years after treatment, and another as living and well two months after treatment. Follow-up data are not given regarding two patients. The best therapeutic result is that already described in the patient reported by Bergstrand,^{6, 7} this boy, age 15, lived six years after removal of the apparently primary costal tumor, and on two occasions very extensive pulmonary metastases disappeared following roentgenotherapy. While successful surgical removal would certainly be possible, should a case be diagnosed and treated before metastases have occurred, it seems likely that roentgenotherapy will be the chief reliance in treatment of Ewing's sarcoma of the ribs. In many instances extensive tumors were present among the listed cases, often with metastases characteristically involving other bones, the lungs, and pleura. Earlier diagnosis should, occasionally, be made if Ewing's sarcoma is borne in mind during the examination of patients complaining of costal pain without apparent cause and with or without palpable tumor. The neoplasm invariably occurs in persons younger than 30 years of age.

Author's Case 10—L. H., white, female, age 22, was admitted, July 16, 1937, complaining of a tumor in the left thoracic region of two and one-half months' duration, that had been called to her attention by severe pain. The tumor had grown steadily. One month before admission she had been delivered of a normal child at term. The patient appeared chronically ill. Just behind the posterior axillary line, overlying and fixed to the tenth, eleventh, and twelfth left ribs was a firm, slightly lobulated, not tender undischarged mass measuring 9x8 cm. No bruit or thrill was present. Roentgenologic examination demonstrated destruction of a portion of the tenth rib and elevation and paralysis of the hemidiaphragm. No Bence-Jones protein was present in the urine, although albumen was.

Examination of the blood disclosed 55 per cent hemoglobin (9.4 Gm.), 4,290,000 red blood cells, 8,100 white blood cells, with 54 per cent polymorphonuclear neutrophils, 21 per cent large lymphocytes, 4 per cent small lymphocytes, 11 per cent monocytes, and 11 per cent eosinophils, with plasma cells present, and platelets in normal quantities. One per cent of the red blood cells were reticulocytes. Dr. Raphael Isaacs, who examined the patient and the blood, stated: "A hypochromic, hyperplastic type of anemia is present suggestive of a chronic nephropathy. Marked eosinophilia is present. Thrombosis should

be expected if operative procedures are used. While the plasma cells are suggestive of a myeloma, hypernephroma should be considered in the differential diagnosis."

Pathologic examination of a specimen from the tumor secured by punch biopsy, demonstrated a round cell sarcoma without evidence of bone formation, which was probably an endothelial myeloma (Ewing's sarcoma) but which might have been a primitive myeloblastoma. Roentgenotherapy was begun and the patient was discharged, the therapy being continued at home. She died shortly afterwards of widespread metastases.

FIBROSARCOMA

Six instances of fibrosarcoma involving ribs are listed in Table VI. The neoplasm probably did not in any case originate in the bones, although it was intimately associated with them at the time of treatment, this sequence is clearly illustrated by Case 12 of this report. Three men and three women from 34 to 61 years of age were affected. The symptoms of the large tumors were of from four months' to four and one-half years' duration. Two patients were treated with roentgenotherapy and the remaining four were treated by operation, with one postoperative death. From this small group of cases the results of therapy are not encouraging, since four patients are dead, one is living with metastatic lesions, and information after operative recovery is not available about one patient.

Author's Case 11—E. P., white, female, age 46, was admitted June 17, 1932. For two years a sensation of heaviness had been present in the posterior, left thoracic region. Since the patient had struck the left chest two months before admission, sharp pain radiating anteriorly was felt. She had noticed a lump, which had reached orange-size, over the left chest posteriorly for one month. The debilitated patient was extremely uncomfortable, and a tender fist-sized tumor was palpable in the region of the left seventh, eighth, and ninth ribs posteriorly. Enlarged lymph nodes were palpable in both axillae and above the left clavicle. Roentgenographic examination demonstrated a soft tissue mass lying over the posterolateral portion of the left thorax, with destruction of segments of the seventh and ninth ribs and erosion of the eighth rib. Pathologic examination of a portion of the tumor removed showed it to be a large cell fibrosarcoma with extensive necrosis. Roentgenotherapy was ineffective in controlling the pain caused by the tumor, which increased in size. The patient was discharged and died in September, 1932, two months later.

Author's Case 12—J. P., white, female, age 50, was admitted March 21, 1935. Four months previously she had become aware of tightness about the right scapula, especially when abducting the arm. During the four weeks prior to admission a mass, which had grown rapidly, was present near the right scapula. On examination, a rubbery, tender tumor, fixed to the deep structures, was palpable between the right scapula and the spinal column, it extended the entire length of the scapula. Roentgenographic study showed a soft tissue tumor over the right chest posteriorly with pressure atrophy or invasion of ribs, especially the third, fourth, and sixth. Right pneumothorax was induced April 8, 1935. Roentgenograms then demonstrated that the tumor extended into the thoracic cavity. The tumor, which was regarded as a neurofibroma, lipoma, or sarcoma, was exposed through a thoracoplasty incision April 12, 1935. Frozen-section examination, of a portion removed, showed the neoplasm to be a fibrosarcoma. The tumor was removed by division and resection of portions of the second to the eighth ribs and removal of the corresponding vertebral spinous and transverse processes with portions of the laminae. The sacrospinalis muscle had been invaded but not the pleura, which was opened widely. The patient died on the fifth postoperative day. Necropsy demonstrated that death was due to bilateral pulmonary atelectasis.

TABLE VI
FIBROSARCOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Dura- tion	Treatment	Result	Histologic Diagnosis	Remarks
(1) Takabatake ¹⁴	M	61	3rd rib anteriorly	Head	Tumor	—	1 yr	Removal with 2nd 3rd 4th ribs	Died a few mos later	Fibrosarcoma	
(2) Takabatake ¹⁴	M	41	8th 9th ribs laterally	Large	Tumor, pain	—	6 mos	Biopsy, x ray	Dying 10 mos later	Fibrosarcoma	Metastases to lungs and lymph nodes present
(3) Speed ¹⁵	F	34	Axillary portion of thoracic wall	Grapefruit	Tumor	—	2 yrs	Removal, Removal with 4 ribs	Death 1 yr, after 2nd operation of pulmonary metastases	Fibrosarcoma	Recurred 6 mos after 1st operation
(4) Cohn ¹⁶	M	42	1st 2nd ribs, anteriorly	Large	Tumor	Pain	4½ yrs	Removal with clavicle and 1st 2nd ribs (previous operation and x-ray therapy)	Survived operation	Fibrosarcoma	History of trauma
(5) Authors' Case 11	F	46	7th 8th 9th ribs posteriorly	Orange	Pain	Tumor	2 yrs	Biopsy, x ray	Death 2 mos later	Fibrosarcoma	Tumor inoperable
(6) Authors' Case 12	F	50	Interscapular region	12x6x6 cm	Pain	Tumor	4 mos	Removal with 2nd to 8th ribs	Postoperative death	Fibrosarcoma	Ribs not actually invaded but surrounded by tumor

Pathologic examination showed the tumor, which passed between the ribs and was closely adherent to them and infiltrated the costal periosteum, to be a spindle cell fibrosarcoma with moderate differentiation

UNCLASSIFIED SARCOMA

Table VII lists data concerning five patients suffering with tumors described as round cell sarcomata, four involving the ribs and one the sternum. Three patients were men, and two women. The ages varied from four to 29 years. Tumor and pain were the only symptoms. One very large tumor of the sternum was merely biopsied, and the four neoplasms of the ribs were resected, with one death due to operation. The most interesting case is that of Hautefort,³⁶ in which the middle lobe of the right lung, adherent to the tumor, was successfully removed, with the tumor and three ribs, from a four-year-old child. No adequate follow-up information is available about these patients other than on the one dying postoperatively.

HODGKIN'S DISEASE AND LYMPHOSARCOMA

Data are given, in Table VIII, regarding four patients with Hodgkin's disease of the sternum and ribs, and two with lymphosarcoma of the ribs. The sex of one patient is not stated, and three were men, and two women. The ages varied from 9 to 39 years. The duration of symptoms of four cases was relatively long—from three to six years, the duration of symptoms of two cases was six months and one and one-half years. Three patients were treated with roentgenotherapy alone, one had an extensive resection of the anterior thoracic wall some time after radiation therapy, one had a limited removal of the involved bones with later roentgenotherapy, and the sixth was treated with excision alone. Three patients with Hodgkin's disease are reported living six, 16 and 18 months, respectively, after treatment, one each with Hodgkin's disease and lymphosarcoma are dead, and one with lymphosarcoma is reported as surviving operation.

In all likelihood the great majority of tumors of the lymphoblastoma group involve the bony thoracic wall secondarily. The close anatomic relationship of the mediastinum to the anterior thoracic wall explains invasion of the sternum and anterior ribs by Hodgkin's disease of the mediastinum. Harrington, Dorsey, and Strohl³⁵ described a Hodgkin's tumor presenting through an intercostal space on the anterior thoracic wall without rib involvement.

Author's Case 13—F. D., white, female, age 28, was admitted March 29, 1934. In September, 1932, 19 months previously, a bulging of the anterior thoracic wall accompanied by dull pain had appeared. After roentgenologic study the mass was incised in July, 1933. Tubercle bacilli could not be demonstrated in the caseous material removed at this time. A therapeutic abortion was performed in October, 1933, because of suspected pulmonary tuberculosis. Several hemoptyses occurred in the months just prior to admission. Examination disclosed a firm orange-sized mass fixed to the sternum at the level of the second and third ribs. A surgical scar ran over the center of the mass, and thin seropurulent material drained from a sinus at its base. Roentgenologic study of the lungs and thoracic wall, in the postero-anterior, oblique, and lateral projections, demonstrated an infiltrating lesion of the anterior portion of the upper lobe of the left

TABLE VII
UNCLASSIFIED SARCOMA

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Dura- tion	Treatment	Results	Histologic Diagnosis	Remarks
(1) Vitale ⁷⁷	M	19	Sternum	Very large	Pain	Tumor	4 yrs	Biopsy	No follow-up	Small round cell sarcoma	
(2) Vitale ⁷⁷	M	23	12th rib	6x3 cm	Tumor	—	—	Removal with 12th rib and soft tissue	Recurrent in 2 mos, and removed again	Round cell sarcoma	
(3) Vitale ⁷⁷	F	29	12th rib	Orange	Tumor	—	3 mos	Removal, with 12th rib	Postoperative death	Small round cell sarcoma	
(4) Hautefort ⁷⁸	M	4	3rd 4th 5th ribs anteriorly	10 cm diam	Tumor	—	6 mos	Removal with 3rd 4th 5th ribs and middle lobe of right lung	Survived opera- tion	Round cell sarcoma of connective tissue origin	Middle lobe of lung adherent to but not invaded by tumor
(5) Martin Henry and Soustelle ⁷⁹	F	26	10th rib poste- riorly	—	Pain	Tumor	More than 1 yr	Removal with 10th rib	Survived opera- tion	Round cell sarcoma	

TABLE VIII

HODGKIN'S DISEASE

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis	Remarks
(1) Fontes ¹ and Abreu ¹	F	39	Sternum	6x3 cm	Tumor	—	3 yrs	Biopsy, x-ray	Well 16 mos later	Hodgkin's disease	
(2) Behrend ²	—	13	1st 2nd ribs with cartilages sternum and clavicle involved	10x8x3 cm	Tumor	—	5 yrs	Previous x-ray, resection with 1st and 2nd ribs, x-ray	Well 1½ yrs later (3 yrs from 1st treatment)	Hodgkin's disease	Little mediastinal disease before operation
(3) Parf Fischegold Abaza and Lewis ³	M	26	Manubrium sterni	Moderate	Pain	Tumor	6 mos	Biopsy, x-ray	Axillary nodes and skin involved 5 mos later	Hodgkin's disease	
(4) Authors' Case 13	F	28	Sternum, 2nd, 3rd costal cartilages	Large	Tumor, pain	—	18 mos	Previous incision, partial excision, x-ray	Died 2 yrs later	Hodgkin's disease	Appearance of associated pulmonary lesion in x-ray suggestive of pulmonary tuberculosis

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LYMPHOSARCOMA

(1) Lowenberg and Ginsberg ⁴	M	9	10th rib	Large	Pain	Tumor	5 yrs	Biopsy, x-ray	Death 6 mos later	Lymphosarcoma	Received serum therapy for hopeless malignancy, experimentally cured
(2) Brun and Cursi ⁵	M	26	9th 10th 11th ribs	20x16x11 cm	Pain	Tumor	6 yrs	Excision with 9th 10th and 11th ribs	Survived operation	Lymphosarcoma	

TABLE IX

MISCELLANEOUS TUMORS

Author	Sex	Age	Site	Size	Initial Symptoms	Other Symptoms	Duration	Treatment	Results	Histologic Diagnosis
(1) Iv. misseviech Egues and Fernandez ⁶	M	17	9th rib posteriorly	7x5x5 cm	Pain	—	7 mos	Excision	Survived operation	Schwannoma
(2) Authors' Case 14	M	27	10th rib posteriorly	—	Pain	—	Some mos	Removal	Well 34 mos later	Fibroma
(3) Authors' Case 15	F	30	5th rib, laterally	5x5x2½ cm	Pain	—	4 yrs	Removal with 4th and 5th ribs, periosteum of 6th rib	Well without recurrence 28 mos later	Neurofibroma

lung with central excavation, which was considered tuberculous. Gross destruction of the manubrium and upper *gladiolus sterni* was present, with involvement of the left second and third costal cartilages. Tubercle bacilli could not be found in smears made from the fluid draining from the sinus. Nevertheless, a diagnosis of tuberculosis of the thoracic wall was made. The tumor mass was, in part, excised and found to be composed of a hard shell of tissue covering a caseous mass that extended into the mediastinum and lung.

The histologic diagnosis of Hodgkin's disease was later confirmed by examination of a lymph node removed from the left axilla. A considerable clinical and roentgenologic improvement followed the administration of 800 units of roentgenotherapy. The improvement continued when the patient was last seen, September 25, 1934, five months after treatment. She died, elsewhere, May 12, 1936, two years after roentgenotherapy.

MISCELLANEOUS NEOPLASMS

Table IX lists data relative to three patients suffering from a fibroma, a schwannoma, and a neurofibroma, respectively. The fibroma was a primary costal tumor, while the schwannoma and neurofibroma were in close relationship to ribs. Case 15 of this report illustrates the close association of a benign tumor of nerve sheath origin to the ribs, which required the resection of two ribs and the periosteum of another with the tumor. The pathogenesis of schwannoma and neurofibroma will not be discussed here. All three patients were treated by operation. The two with fibroma and neurofibroma are living and well 34 and 28 months, respectively, after operation and the one with schwannoma is reported merely as surviving operation.

Author's Case 14—A. A., white, male, age 27, was admitted, December 21, 1932, complaining of pain in the back and knees of some months' duration. Roentgenograms of the spine, which confirmed the clinical diagnosis of arthritis, revealed also a tumor of the posterior portion of the left tenth rib. Further roentgenographic study (Fig. 12) demonstrated the homogeneous, expansile tumor covered by a thin shell of calcified tissue. The tumor, which had not broken through its bony cortex, was removed with the adjacent portions of the left tenth rib, January 9, 1933. The pleura was not opened. The patient was discharged some time later after treatment of the arthritis.

The pathologic diagnosis was a very cellular fibroma approaching a spindle cell sarcoma. November 23, 1935, 34 months after operation, the patient was well, without recurrence of the tumor.

Author's Case 15—V. W., white, female, age 30, was admitted February 4, 1938. A roentgenographic examination (Fig. 13), December 10, 1937, had been made because of discomfort in the chest and had revealed a circumscribed mass in contact with the fourth to sixth ribs in the right posterior axillary line. Two and one-half years previously, the patient had had an attack of pleurisy with effusion. No change in the mass, which was associated with slight irregularity of the fourth rib, was noted in another study one month later. Physical examination of the patient found no evidence of a thoracic wall tumor. The diagnoses considered were tuberculous abscess, pulmonary tuberculosis, and primary or metastatic tumor. February 3, 1938, the tumor, together with the adjoining segments of the fourth and fifth ribs and the periosteum of the sixth rib, was removed. The tumor, which extended beneath the sixth rib, was dissected bluntly from the lung. Aspiration before section of the ribs had demonstrated the mass to be solid. The patient was discharged 11 days after operation.

The specimen consisted of portions of two ribs seven and one-half and nine centi-

meters long, respectively, with an encapsulated tumor, 5x3 cm, firmly attached to one rib. Microscopic examination showed the tumor to be a neurofibroma, probably arising from an intercostal nerve, although this could not be definitely demonstrated, the ribs were not involved. The patient was quite well in May, 1940, 28 months after operation.

METASTATIC TUMORS

During the study of the hospital records many instances of malignant tumors, metastatic to the ribs, were found. The sites of primary origin were



FIG 12—Case 14. Posteroanterior roentgenogram of fibroma of left tenth rib.

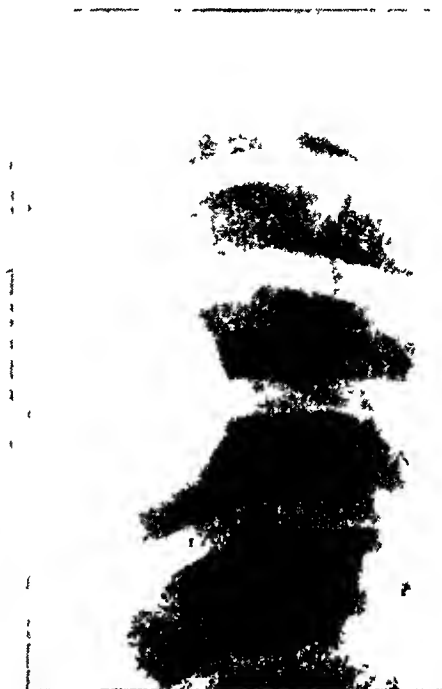


FIG 13—Case 15. Posteroanterior roentgenogram of neurofibroma, closely adherent to the right fourth, fifth, and sixth ribs.

in many different organs. In several cases the metastatic costal tumors were the presenting lesions. Cline¹⁷ has discussed pulsating tumors of the sternum, metastatic from carcinomata of the thyroid and kidney. Roth and Davidson⁶⁷ have reported an additional case of pulsating sternal tumor secondary to an hypernephroma.

SUMMARY

Data have been presented regarding 66 cases of neoplasms of the bony thoracic wall, collected from the literature since 1933, and 15 cases from the University of Michigan Hospital, the collected cases include two of Ewing's sarcoma reported by Geschickter and Copeland,²⁷ in 1931, and not included in Hedblom's³⁹ 1933-report. In considering benign giant cell tumor and Ewing's sarcoma, an effort has been made to gather all known cases from the literature, four and three cases, respectively, were reported prior to 1933, in addition to the two mentioned. These seven cases were included by Hedblom.³⁹

The treatment of the great majority of tumors of the bony thoracic wall

has been by operation, at which an effort was usually made to remove the neoplasm completely. In some instances several operations were performed. Twenty-seven cases of benign tumors (osteomata, chondromata, benign giant cell tumors, fibroma, schwannoma, and neurofibroma) reported since 1933, were treated surgically, with one death due to operation (3.7 per cent). Thirty-six malignant tumors (osteogenic sarcomata, Ewing's sarcoma, fibrosarcoma, unclassified round cell sarcomata, Hodgkin's disease, and lymphosarcoma) reported since 1933, were treated by operation with three deaths due to operation (8.5 per cent). Radiation therapy was employed in conjunction with surgery in a number of instances. Fourteen patients (seven of them with Ewing's sarcoma) were treated with radiation alone, and two patients received no treatment whatever.

Although extensive follow-up information is, unfortunately, not available for any group of cases except those of benign giant cell tumor, some conclusions as to the results of therapy may be drawn. The greatest therapeutic success has been obtained in benign giant cell tumor, with five cures of more than ten years' duration, and one of more than five, four of the cures of long duration are in patients reported prior to 1933. Among the patients with chondromata, there are three five-year cures, and three patients are living and well more than two years after operation. One patient, who was operated upon for an osteoma, is living and well, two years later, and patients with a fibroma and a neurofibroma are well 34 and 28 months, respectively, after operation. The striking fact about the 33 patients with benign tumors is that only three are reported as dead.

Among the malignant tumor groups there is no case with a five-year cure, and only two of osteogenic sarcomata with three-year cures. The most discouraging group from the standpoint of therapy, is that of Ewing's sarcoma, with 14 of 18 patients reported dead, and one reported living with recurrence, adequate follow-up information is not available relative to the other three patients. Of the 20 patients with osteogenic sarcoma, six are reported as dead, and five as living, with recurrent and metastatic tumors. Four of the six patients with fibrosarcoma are reported as dead, and a fifth as living, with metastases.

Long periods of follow-up are not given for the five patients with unclassified sarcomata, and the six patients with tumors of the lymphoblastoma group, although one and two, respectively, are known to be dead. There is a marked difference in the results obtained from treatment of the benign and malignant groups of tumors affecting the ribs and sternum. Twenty-seven of the 55 patients with malignant tumors are known to be dead.

Complete surgical removal of tumors of the ribs and sternum appears to be the most effective form of therapy. The mortality of surgical treatment of these tumors has been low in recent years. Very extensive operations have been carried out successfully to remove huge tumors, even those directly involving the lung. Roentgenotherapy has been ineffective, except in two cases.

of benign giant cell tumor and, palliatively, in one case of metastatic Ewing's sarcoma

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AUTOPLASTIC TRANSPLANTATION OF SPLENIC TISSUE, IN MAN, FOLLOWING TRAUMATIC RUPTURE OF THE SPLEEN

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AT THE HILLMAN HOSPITAL, Birmingham, Ala., during a seven-year period, from 1933 through 1939, there were 457 cases with acute abdominal injury, including penetrating wounds, as well as subcutaneous injury, admitted to the hospital. Among these cases, only 17, or 3.7 per cent, of the whole number, were instances of traumatic rupture of the spleen. According to Berger,³ about 51 per cent of individuals who experience acute rupture of the spleen, die of hemorrhage within one hour of the accident. Of those that survive this primary mortality, 15 to 55 per cent will die within a few days, in spite of the best modern surgical treatment for acute traumatic rupture of the spleen. Besides this, there is a huge fatality rate of 90 to 100 per cent, for individuals suffering such an accident, who refuse, or do not receive surgical intervention. Consequently, human survivals of traumatic rupture of the spleen are, indeed, small in number. The chances of a person in this group of survivals, either having an abdominal surgical exploration, or coming to autopsy examination at some future date, would be proportionally much less, which may account for the rare disclosure of the condition which was found upon postmortem examination of the abdomen, in the case to be described. The numerous spleen-like nodules found scattered over the peritoneum, including the surfaces of the omentum, small and large bowel, the diaphragm, and the pelvic cavity, were not accessory spleens, but small splenic implants. These implants grew from viable splenic pulp cells dispersed over the peritoneal cavity, as a result of the intra-abdominal splenic hemorrhage, when this normally vascular organ ruptured. Some of these viable cells, normally situated in the splenic parenchyma, were torn away by the force of the trauma and bleeding, to float with the hemorrhage to a new location, and graft themselves diffusely on living peritoneum. With the passage of time, a fibrous reaction, or capsule, formed about these nests of splenic cells, as they underwent division and growth, in their new beds. Parenchymatous cells of no other abdominal organ are known to exhibit similar characteristics, excepting, possibly, the uterine endometrium.

Case Report—Hosp No 101843 H M, colored, male, age 9, entered Division A, Surgical Service, Hillman Hospital, September 30, 1935, about five and one-half hours after he had fallen out of a tree, striking his abdomen on the ground. Abdominal pain

AUTOPLASTIC SPLENIC IMPLANTS

was immediately complained of, mainly in the region of the umbilicus. He had not become unconscious, nor had he vomited. There had been no gross hematuria.

Physical Examination—Temperature, per rectum, 100.6° F pulse, 152, blood pressure 90/54. The patient appeared apprehensive, with tense nares, and rapid, shallow respirations. Lungs were negative. The abdomen was moderately distended, and rigid. There was general abdominal tenderness on palpation, which was more marked in the left upper abdominal quadrant, and left flank. An increase in flank dullness was noted, which seemed to shift.

Hemoglobin 50%, R B C 3,010,000, W B C 15,500, with 89% neutrophils, and 11% lymphocytes. Urinalysis 150 mg albumin, microscopically, a few granular casts, together with four to six leukocytes, and 50 to 60 red blood cells per high power field. One hour later, the hemoglobin was 49%, R B C 3,000,000. The pulse becoming more rapid. *Clinical Impression* Ruptured abdominal viscus, exploratory celiotomy advised. Before operation 1,000 cc of normal saline was administered by hypodermoclysis.

Operation—R A H. Two and one-half hours after admission. Under ether anesthesia, the abdomen was opened through an upper left rectus incision. A large amount of free blood was found present, and the spleen was found to be ruptured, almost in half, with active bleeding. A splenectomy was rapidly performed. No spleen-like nodules were noted within the abdomen. During operation intravenous gum acacia solution was administered, and this was immediately followed by a blood transfusion.

TABLE I
SERIAL BLOOD COUNTS*

Date	Hemo- globin	Red Blood Cells	Color Index	Leuko- cytes	Neutro- phils	Lymphi- cytes	Large Mono- nuclears	Eosino- phils	Baso- phils	Time Relation to Operation
9/30/35	50%	3,010,000	0.8	15,500	89%	11%				On entrance Preoperative
9/30/35	49%	3,000,000	0.8							1 hour later
10/ 1/35	45%	2,720,000	0.8	12,950	86%	14%				1st day, P O After blood transfusion
10/ 7/35	37%	2,530,000	0.7							P O 7th day
10/10/35	40%	2,150,000	0.9							P O 10th day
10/14/35	65%	3,560,000	0.9	14,050	82%	12%	3%			P O 14th day After blood transfusion
10/17/35	47%	2,460,000	0.9	6,350	55%	43%		2%		P O 17th day

* In the case reported. These were taken during the patient's first stay in the hospital as a result of the acute traumatic rupture of the spleen.

Except for some abdominal distention during the early postoperative phase, which was combated with a stomach tube, and the presence of a secondary anemia, the convalescence was essentially uneventful. The wound healed per primam, and the dressing was removed 13 days after operation.

Second Admission—Thirty-nine months later, on January 1, 1939, when the boy was age 13, he was again admitted to the Hillman Hospital, on the Medical Service, Hosp No 127278, with a clinical diagnosis of acute tetanus, contracted from an injury of his left little finger by the explosion of a firecracker on December 25, 1938, six days previously. In spite of energetic treatment with tetanus antitoxin, the patient died 20 hours after he entered the hospital. An autopsy (Dr J D Bush) was performed two and one-half hours after death. Only a portion of the complete autopsy report will be included.

Postmortem Examination—(A-39-2) The changes of greatest interest were limited to the thoracic and peritoneal cavities. The upper anterior mediastinum was filled by a bilobed thymus gland, which weighed 61 Gm. The tracheobronchial lymph nodes were large and contained black pigment. There were several fibrous adhesions binding the healed splenectomy wound to various loops of bowel and to the omentum. There were numerous adhesions about the splenic bed and one spleen which measured 3 by 4 cm. was firmly adherent to the splenic bed. Scattered over the abdomen were several dozen firm, dark red nodules which measured from 0.5 to 1 cm. in diameter. These were found on the inferior surface of the left dome of the diaphragm, the omentum, the small bowel, the ascending colon, the transverse colon, the descending colon and over the pelvis including the anterior surface of the rectum and the rectovesical pouch. The smaller ones were rounded, the larger ones were flat and measured 0.2 to 0.3 cm. in thickness. All were sessile and covered with serosa. In color and consistency they closely resembled splenic tissue. The surface was red and on section there was a thin, white fibrous capsule enclosing a firm, dark red, spleen-like tissue. The total number of the nodules was approximately 75.

Pathologic Examination—Microscopic—Sections of the nodules revealed a structure morphologically similar to adult spleen. Each nodule was surrounded by a capsule composed of fibrocytes and collagenous fibers. The convex surface of the capsule was covered by a layer of flattened endothelial cells continuous with the serosa of the structures to which the implant was attached. In the capsule there were scattered foci of lymphocytes, particles of iron pigment and small blood vessels filled with erythrocytes. Trabeculae extended from the capsule into the pulp, occasionally traversing the entire width of the nodule. These trabeculae possessed a structure similar to the capsule and were accompanied by small blood vessels. There were a number of follicles present, each composed of lymphocytes, in a few an arteriole was also present. No germinal centers were evident. The red pulp was composed of sinuses lined by a single layer of cells with prominent nuclei. The sinuses were filled with erythrocytes, polymorphonuclear, neutrophils and a few endothelial leukocytes. An occasional siderophage was seen in the red pulp.

Discussion—In medical literature, there apparently have been only ten similar cases described. Two other autopsy examinations were reported, in which spleen-like nodules were so diffusely scattered over the abdominal cavity, as to practically rule out the author's diagnosis of accessory spleens. These two last mentioned autopsy examinations were made on individuals who gave no history of trauma, and had not undergone a splenectomy. However, in both instances the spleen and surrounding area presented gross findings, usually associated with residuals from healed trauma. Consequently, one might well reason that these cases represented splenic implants from traumatic splenic ruptures which had healed, and will be so considered. Table II briefly summarizes the 12 cases described in the literature, as well as our own case. Only three such cases have been reported in American medical literature, and these were published since September, 1939, two of these were by the same author. A detailed review of the earlier reported cases is made in the excellent articles by Shaw and Shafi, Jarcho and Anderson, and Buchbinder and Lipkoff. Buchbinder and Lipkoff recognize Foltin, who described a case in 1911, as being the first to suggest that the spleen-like nodules in question, were splenic implants. These same two authors wished to designate this entity of autoplasmic transplantation of splenic tissue as "splenosis."

FIG 1

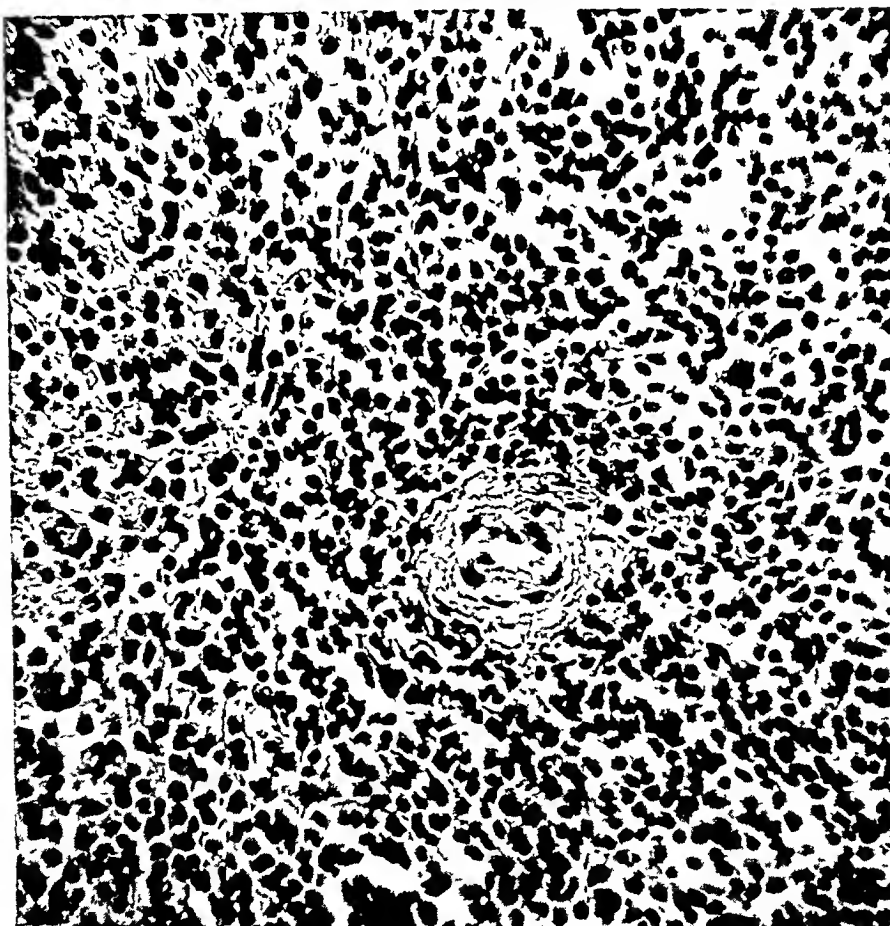


FIG 2

FIG 1—Photomicrograph of a full section of autoplasmic splenic transplant, from the case reported, showing capsule, trabeculae, malpighian corpuscles, and pulp. On one surface it is adherent to the diaphragm (Hematoxylin and eosin) ($\times 10$)

FIG 2—Photomicrograph of the same section as shown in Figure 1 showing a central arteriole, surrounded by lymphocytes, and a portion of splenic pulp (Hematoxylin and eosin) ($\times 176$)

TABLE II
SUMMARY OF REPORTED CASES OF AUTOPLASTIC TRANSPLANTATION OF SPLENIC TISSUE

Author	Date	Sex	Age at Time of Diagnosis	Age at Time of Rupture of Spleen	Reason for Splenectomy	Time after Splenectomy	Location of Nodules	Number	Size of Implants
Albrecht	1896	Male	25	?	Autopsy	No history of trauma or splenectomy	Greater omentum, rectovesical pouch, and both domes of diaphragm	Numerous	Not stated
Schilling	1907	Female	47	?	Autopsy	No history of trauma or splenectomy	Greater omentum, peritoneum of anterior abdominal wall, and of pelvis	12 on greater omentum (several more)	Pea to cherry in size
von Kuttner	1910	Male	?	?	Autopsy	4 years	Scattered throughout the peritoneum	80 to 100	Not stated
Foltin	1911	Male	9	3	Chronic appendicitis	6 years	On loops of large and small intestine	Numerous	Lentil to cherry in size
von Stubenrauch	1912	Male	?	?	Ileus	10 months	Greater omentum, transverse mesocolon, and small intestine	Numerous	Hemp seed to pea in size
Oltman (quoted by von S) Lee	1919 1923	?	?	?	Not stated	Not stated	Throughout peritoneal cavity	Multiple	Not stated
		Male	29	14	Ileus	15 years	Small intestine and mesentery	Numerous (200-300)	Pin head to 1½ inches
Kupperman	1936	Male	15	14	Postoperative hernia	6 months	Small and large intestines	100	Not stated
Shaw and Shufi	1937	Male	20	?	Autopsy	Not stated	Abdominal wall, pleural cavity, liver diaphragm, rectovesical pouch and great omentum	82	0.2 to 2 cm
Jarcho and Anderson	1939	Male	8	6	Autopsy (ileus)	18 months	Left dome of diaphragm, liver, stomach, lesser omentum, transverse colon, rt kidney, rectum, and bladder	Several dozen	1 to 12 Mm in diameter Larger nodules 2 to 3 Mm in thickness
Jarcho and Anderson	1939	Male	20	12	Autopsy	8 years	Peritoneum, greater omentum, diaphragm, greater curvature stomach	80	1 Mm to 3 cm in diameter
Buchbinder and Lipkoff	1939	Female	28	8	Pelvic operation	20 years	Parietal peritoneum, great omentum, ileum, sigmoid, and ascending colon	Numerous	1 Mm to 2 cm in diameter
Authors	1940	Male	13	9	Autopsy (tetanus)	39 months	Parietal peritoneum, pelvic cavity, omentum, serosa of large and small bowel, diaphragm	Approx 75	0.5 to 1 cm in diameter

The first group of writers who published case reports, which appear to come in this category, diagnosed the nodules as being either accessory spleens, or tissue derived from embryologic spleen-forming rests, contained within the peritoneum. Spleen-forming rests most likely would be found only in tissues or structures closely approximated to the splenic area in embryologic development. Accessory spleens would be the logical outgrowths from these fetal splenic rests, should they take on a growth stimulus. As to the prevalence of accessory spleens, Adam and Nichols found them in 11 per cent of a series of autopsy examinations. These bodies probably are more often observed in young individuals, than in adults. Jolly states that 25 per cent of children, less than seven years of age, had accessory spleens. Sos-suchin observed them in 15 per cent of 153 children, less than ten years of age. Additional mention is made that their diminished occurrence in adult life is possibly due to atrophy. The size of accessory spleens varies from a few millimeters to several centimeters in diameter. Accessory spleens present the same histologic structure, and are subject to the same pathologic alterations, as the main organ. Usually, not more than one to six accessory spleens are present in any one case. These bodies, as mentioned above, are mainly found only in tissues adjacent to the splenic area in fetal development, such as the splenic fossa, gastrosplenic ligament, pancreaticosplenic ligament, pancreas, and the great omentum. The large splenic nodule found within the splenectomy bed, at postmortem examination in our case, no doubt, was a true accessory spleen.

The cases reported in medical literature which show splenic implants reveal that these splenic grafts have been found growing on a portion of almost every area of the peritoneal cavity as well as on the contained viscera. In all the reported cases with splenic implants, there are described numerous spleen-like nodules, surrounded by a fibrous capsule of variable thickness, enclosing tissue much like splenic pulp, which may, or may not, have lymph follicles. Any follicles present may be rudimentary in appearance, consisting of a few lymphoid cells surrounding a central arteriole, or they may be well-developed mature follicles. In some instances definite little blood sinus formations are present. Fibrous septa tend to infiltrate the enclosed cellular mass, from the surrounding capsule. A well-developed hilum is absent. The blood supply is from small arterioles which enter the nodule irregularly, from the surrounding tissue, at various points through the fibrous covering. Enveloping the whole nodule is serosa. Apparently, any function that these transplants might have, would be that of the normal splenic pulp.

Grossly, the splenic implants have been found to be both sessile and pedunculated, and to have a nodular, spherical, or flattened shape. They have varied in size from 1 Mm to 3 cm in diameter. In color and consistency, the nodules have the appearance of splenic tissue. Colors described for these transplants are normal spleen color, dark red, purple-red, and greenish-black. In one instance, that reported by Buchbinder and Lipkoff, the sur-

geon first discovered many small purple-red nodules, scattered over the peritoneum and viscera during the course of a female pelvic operation, and mistook their appearance for endometriomata, until microscopic diagnosis of an excised nodule revealed their true nature. The highest numerical estimate for these transplants was 200-300 in one case. In another instance, the base of the left pleural cavity was invaded. Probably this invasion occurred through a small rent in the diaphragm, which happened at the time of the accident, and later healed. No subcutaneous transplants within the operative wound scar have been reported. However, splenic grafts have successfully taken in the subcutaneous tissues of animals, when experimentally transplanted, as demonstrated by Maine and Manley, Perla, and others.

An interesting case is reported by Jaicho and Anderson, in which about 400 cc of hemorrhagic blood was removed from the peritoneal cavity, at the time of operation for an acute traumatic rupture of the spleen, and immediately citrated, strained through gauze, and reinjected intravenously into the patient. Eight years later, at the age of 20, the patient died from acute perforated appendicitis. On postmortem examination, there were discovered 80 splenic transplants scattered over the peritoneum but no splenic nodules were found in the lungs, or outside the abdominal cavity. Nevertheless, the possibility of viable splenic cells contained in hemorrhagic blood obtained from the abdomen for retransfusion in such patients should be kept in mind.

Kreuter, in 1920, experimentally excised the spleen in monkeys, and then smeared the splenic pulp over the peritoneum. Several weeks, or months, later, the animals were sacrificed and splenic nodules were found widely dispersed over the peritoneal cavity. Jaicho and Anderson review literature giving instances of dogs who had a history of severe abdominal trauma, and later following death, postmortem examination revealed nodular implants of splenic tissue scattered over the abdominal cavity. These authors also observe that Griffin and Tizzoni, as early as 1883, related that partial splenectomy in dogs was followed by development of spleen-like nodules in the peritoneum.

So far as we were able to ascertain, no cases have been reported in which there were widely disseminated splenic nodules following splenectomy, for nontraumatic diseases of the spleen. Shaw and Shafi express the opinion that the removal of diseased spleens, apparently is rarely, if ever, followed by implants, in spite of occasional tearing, with some associated hemorrhage, during the excision of large splenomegalies.

In the spleens of individuals, past the age of 30, Gross finds that the nuclei of the fibroblasts disappear, and the fibrils become thickened and few. Likewise, the intima and media of the blood vessels within the parenchyma become thickened with connective tissue and hyaline changes. Wohl calls attention to the gradual collapse of lymph tissue, from birth onward. Because of the changes, mentioned above, he believes there occurs a decrease

in the power of constructive metabolism, which factor contributes to the rather early senescence of the organ

The average known age at the time of the traumatic rupture of the spleen, among all the reported cases of autoplasmic transplantation of splenic tissue including ours, was nine plus years. It appears to us quite significant that the youngest was age three, and the oldest was 14 years. We believe the likelihood of successful grafting of these cells on a peritoneal surface is proportionate to the youthfulness of normal splenic tissue which has been traumatically ruptured. Pulp cells from the spleen of young individuals, very likely, possess properties of increased viability, or virulence, differing from similar cells in the adult spleen. We are of the opinion that such splenic implants may be found more often after traumatic rupture of the spleen, in young individuals who survive, than is generally recognized, and probably such a response is more the rule than the exception.

As yet, no symptoms have been known to result from these splenic implants. That the opportunity offered to discover such a condition in man, is minimum, was remarked in the early part of this discussion. Jarcho and Anderson, more concretely, emphasize this circumstance in their review of the last 2,000 autopsies at the Babies Hospital in New York, by finding only nine cases who had undergone a previous splenectomy for various reasons, from a few hours to nine years prior to autopsy. The only case in which operation had been performed, because of traumatic rupture of the spleen, was one of their published cases of autoplasmic transplantation of splenic tissue. Then again, out of 2,605 autopsies at the Presbyterian Hospital, in New York, during a ten-year period, these same authors found that splenectomy had been performed in 16 cases, from two weeks to 16 years, prior to autopsy. There were no instances of splenectomy for traumatic rupture of the spleen in this group, and none revealed splenic tissue, other than the finding of an accessory spleen, or so, in the bed from which the spleen had previously been removed. Finally, Shaw and Shafi observe that out of a series of 708 cases of splenectomy, published up until 1908, and 417 cases reported by Mayo in 1926, no pathologic studies of the late results of splenectomy are mentioned.

SUMMARY AND CONCLUSIONS

(1) A human case is reported which developed nodular splenic implants throughout the peritoneal cavity, following traumatic rupture of the spleen. This is the thirteenth case of similar nature, in man, described in medical literature. A chart summarizing these cases is appended.

(2) A detailed discussion of autoplasmic transplantation of splenic tissue, is made.

(3) It is our opinion, that in man relative youthfulness of normal splenic tissue is a very important factor, as regards viability of splenic pulp cells for autoplasmic implantation, and the likelihood of successful grafting of these cells on a peritoneal surface following traumatic rupture of the spleen.

(4) Autoplastic transplantation of splenic tissue may be more the rule than the exception in individuals who have suffered a traumatic rupture of the spleen, in their youth, and have survived the accident

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AN UNUSUAL CASE OF BENIGN MULTIPLE CHORIONIC VILLI IMPLANTS IN PERITONEAL CAVITY ACCOMPANIED BY HEMOPERITONEUM

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TO CLEARLY UNDERSTAND the significance of the case about to be reported, it would not be amiss to review the subject of chorionepithelioma. Chorionepithelioma is a malignant tumor originating from, and confined to the epithelium of the chorionic villus, which differs from the hydatid mole in that in the latter there also occurs an accompanying proliferation of the villus stroma. As is well known, this neoplasm may arise from the chorionic villus at term, in cases of abortion or from an hydatid mole. While the usual site of growth is the uterine cavity, it has been known to take origin in the fallopian tube (Walsh,²⁰ Phillips,¹² Moore¹¹). In rare instances the site of origin could not be determined, since the uterus and adnexa have been found normal in cases where the manifestations of the disease resulted from distant metastases. In a few cases the site of origin of the chorionepithelioma has been a teratomatous tumor in an ovary or testis.

While Chiari,² as far back as 1877, was the first to describe three cases of carcinoma of the uterus which have subsequently been classified as chorionepitheliomata, it was not until 1895 that Maichand⁹ first recognized that such tumors were of epithelial nature and that their site of origin was the placenta.

Pregnant women during childbearing period are most frequently affected. Cases, however, have been reported during the menopause, and in rare instances in young virgins. Several cases have also been reported in the male where the tumor has taken its origin in a teratoma of the testis. A review of the literature disclosed the fact that in the great majority of cases, the tumor manifests itself between one and four months after full term labor, abortion, or the expulsion of a mole.

The characteristic feature of an uterine chorionepithelioma is a nodular or fungating, friable tumor presenting a distinctly hemorrhagic appearance, with evidence of infiltration of the uterine wall. The tumor may penetrate the wall of the uterus and invade the peritoneum. The macroscopic appearance of an extra-uterine chorionepithelioma is that of a tumor resembling an hematoma, presenting no anatomic relationship to the site of a preexisting placenta, located anywhere in the peritoneal cavity, portio vaginalis, broad ligament, or the vagina. The general consensus of opinion is that such a tumor probably arises from a primary uterine tumor which has either undergone regression or has been expelled with its placenta. von Zalke,¹⁹ however,

states that such extra-uterine chorionepitheliomata may arise from cells which have been extruded through the tube from a possible normal intra-uterine placenta. Cases have also been reported of chorionepitheliomata arising in the fallopian tubes (Georgii,⁷ Solomons and Smith¹⁶)

Sunde¹⁸ reported a case of chorionepithelioma arising from an ovarian pregnancy. Pick,¹³ discussing the problem of ovarian chorionepithelioma, maintains that, as a rule, such tumors arise from preexisting teratomata, without the presence of pregnancy.

In differentiating between the histologic features of the constituents of a normal chorionic villus and that of a villus from a chorionepithelioma, we find in the latter that the cells show a greater tendency to invade blood vessels, to produce a ferment with properties of causing tissue dissolution, and to cause vasodilatation of surrounding capillaries. Both types of villi contain Langhans' cells and syncytium, and it was Marchand⁹ who first proved that the chorionepithelioma took origin from the trophoblast.

Microscopically, a typical chorionepithelioma discloses Langhans' cells which appear as well circumscribed polygonal cells with large nuclei. Among these cells one sees groups of darker-staining multinuclear cells or sheets of cells—syncytium, along with numerous blood sinuses, some of them containing tumor elements. Hemorrhagic islands and areas of scattered necrosis are characteristically seen in these tumors. Rarely does one encounter well-defined villi in chorionepitheliomata. Alveolar arrangement of the cell groups makes up the usual mosaic of such tumors. Invasion of surrounding musculature is readily discernible by the presence of islands of tumor cells dispersed among the muscle fibers. The presence of old blood, fibrin and leukocytes can be seen surrounding the site of the tumor. Invasion of the existing blood vessels by tumor tissue is not uncommon. Tumors vary widely in their contents of Langhans' cells and syncytium, some chorionepitheliomata having a preponderance of Langhans' over syncytium, and *vice versa*. In contradistinction to the normal chorionic villus, one notes in chorionepitheliomata a greater variation in the size, shape and staining qualities of the individual Langhans' cells and a greater likelihood of mitotic figures within the cell nuclei.

Although Ewing³ maintains that one can give a fairly accurate prognosis based upon the histologic features of a given tumor, the consensus of opinion to-day is that such histologic groupings are unreliable as a prognostic index (Schlagenhaufen,¹⁵ Frank,⁵ Frank and Geist⁶)

Chorionepithelioma is notorious for its tendency to metastasize early. This is due to the close proximity of the tumor tissue to blood sinuses and to the marked tendency of the neoplastic tissue to invade blood vessels. The sites of predilection of such metastases are the lungs, vagina and vulva. The histologic structure of metastases closely simulates that of the parent tumor, and only in rare instances have distinctly formed villi been found (Miller¹⁰)

Uterine bleeding is by far the outstanding symptom of chorionepithelioma, and may appear during or after the termination of pregnancy. At times,

bleeding may be severe enough to cause exsanguination and death, but, usually, bleeding is more or less intermittent. Cases have been reported where the initial symptoms manifested themselves as a result of metastases (Kedzierski,⁸ Stiaume¹⁷). In any event, the persistence of vaginal bleeding following a miscarriage or a normal labor should arouse suspicion that such a condition might be present. A carefully performed curettage definitely establishes the diagnosis.

At the present time, great reliance is being placed upon biologic tests to determine the presence and course of a given case of suspected chorionepithelioma. Frank and Geist⁶ report no false positive reactions in their extensive experience with the Aschheim-Zondek test in mice, or with the Friedman tests on rabbits. However, in less than two per cent of their cases these same investigators have noted a negative reaction which turned positive after an interval of two or more weeks.

While it is true that the diagnosis of chorionepithelioma usually carries with it a grave prognosis, one must be extremely guarded in following this rule in a given case, since it is well known that the disease discloses great variation in its virulence. Cases have been reported where the disease followed a fulminating course, while others have been noted to show spontaneous regression (Rockafellow¹⁴). Such variations in behavior of chorionepithelioma may of course have been due to errors in properly interpreting histologic sections. With the present use of biologic tests, however, such errors will most likely be greatly avoided. According to Frank and Geist,⁶ the most virulent tumors are those originating in the fallopian tube, ovary and testis.

Case Report—M. L., age 23, was seen in consultation on February 18, 1940, complaining of severe pain and tenderness in the lower abdomen of one day's duration.

The family history was irrelevant. Two years previously she had been delivered of a dead fetus, at term. Following the delivery her periods returned to normal, until December 20, 1939, when she skipped a period. This amenorrhea was attributed to pregnancy and an abortion was performed January 20, 1940. There was no staining or bleeding following the curettage. On and off, for the past three months, she complained of pain in the lower abdomen. For the preceding 24 hours, however, the pain in the abdomen had become severe and was accompanied by nausea.

She was admitted to the hospital February 18, 1940, where a physical examination disclosed a pale, poorly nourished young woman, appearing acutely ill. Save for the abdominal and vaginal findings, the physical examination was essentially negative.

Abdominal examination disclosed a moderately tender, soft abdomen, with a positive rebound. Vaginal examination disclosed a small, apparently normal, freely movable uterus, with suspicious fluctuation in both fornices. Temperature 99° F, pulse 80. Leukocytes 16,300, 88 per cent polymorphonuclears, and 12 per cent lymphocytes. The urinalysis was essentially negative. Suspecting that we were dealing with a surgical abdomen, probably due to an acutely inflamed appendix, celiotomy was advised and accepted.

Operation—Under spinal anesthesia (tropacocaine), the abdomen was opened through a three-inch right lower Kammerer incision. Upon incising the peritoneum, one noted a large amount of blood and several large clots in the peritoneal cavity. The uterus appeared small, was of normal consistency, and to all intents and purposes normal in every

way The left adnexa disclosed a few, small bead-like nodules on the outer surface of the tube, but appeared otherwise normal, while the right fallopian tube was studded with small dark-purplish nodules, giving the tube the appearance of a string of colored beads The ovary was closely adherent to the tube, but one could not ascertain any distinct evidence of rupture either of the tube or ovary to warrant the assumption that we were dealing with a ruptured ectopic pregnancy Blood, however, seemed to be oozing from the right tube

After thoroughly evacuating the peritoneal cavity of blood and clots, one noted several nodules of a dark-purple color, varying in size from beads to small hazel nuts, studding the serosa of the small and large bowel and omentum The appendix appeared slightly injected and thickened, with a bulbous tip The right tube and ovary were extirpated along with the appendix A portion of omentum containing a few large nodules for histologic study was also removed between mass ligatures The abdomen was closed in layers

Postoperative Course—On the evening of the twenty-second, 450 cc of citrated blood was administered intravenously Save for a feeling of marked asthenia, the post-operative course was uneventful A blood count, taken February 26, showed 4,000,000 R B C , 7,700 W B C , with 60 per cent polymorphonuclear leukocytes, and 40 per cent mononuclear cells, hemoglobin 70 per cent Two days later the hemoglobin rose to 82 per cent The wound healed by primary union and the patient was discharged March 2, 1940

An Aschheim-Zondek test taken while the patient was still in the hospital was positive Four successive A-Z tests performed subsequently, at weekly intervals beginning March 5, 1940, were all negative

Pathologic Examination—*Gross* Dr A Schifrin Specimen consists of two masses (1) A portion of omentum measuring 7x4 cm There are four hemorrhagic, spherical masses present, varying from pea- to cherry-size On section they consist of clotted blood within which no cellular tissue is noted grossly, except for occasional greyish-pink dot-like fragments of friable tissue The peripheral zone fuses with the areas of interstitial hemorrhage In adjacent portions there are fibrinous adhesions and curling of the omental surface (2) A tube and ovary with tubo-ovarian ligament The ovary is the size of a walnut and is but slightly enlarged The surface shows several split pea and smaller hemorrhagic nodules which, on section, seem to be superficial and do not seem to arise from within the ovary The ovarian parenchyma shows fibrosis and several follicular cysts and involuting corpus luteum The tubo-ovarian ligament contains a pea-sized and several smaller nodules which are fully covered by the peritoneal reflection The latter appears bluish but not ulcerated or perforated On section, the nodule consists of an hemorrhagic, rather well-localized mass which contains greyish-pink cellular tissue This mass is not in communication with the tubal lumen but is in contact with the outer wall of the latter There are several similar smaller nodules, some close to the peritoneal reflection, but more penetrating it The tube is of normal size, slightly edematous, and the lumen contains pale white mucosal folds which fill the latter The lumen is not dilated and contains no blood The fimbriated extremity is normal

Microscopic—*Omental Hemorrhagic Mass* (Fig 1) This mass is the largest of the omental masses and is 2.5 cm in diameter Its central portion is occupied by clotted blood consisting of dense platelet masses and extravasated intact red blood cells with scattered polynuclear leukocytes and lymphocytes Within the meshes of the clot, typical degenerated chorionic villi are seen composed of a central zone of myxoma-like stroma with poorly staining nuclei and a bright pink peripheral syncytial layer containing occasional necrobiotic and pyknotic nuclei At the periphery of the bloody mass there are more typical chorionic villi which, however, are intact and stain well They consist of a central zone of loose myxoma-like stroma with well-stained, spindle-shaped and vesicular nuclei The peripheral layer of the villi is composed of a single row of cuboidal-



FIG 1—Section from larger hemorrhagic omentum mass (A) Omental fat tissue showing interstitial hemorrhage and mild fibroblastic, round cell and leukocytic reaction (B) Wall of the mass showing fibrosis and scant decidual reaction (C) At left and above, several chorionic syncytial elements with regular nuclei (D) Extravasated blood with darkly staining chorionic wandering cells at left, and pale decidual cells above D (E) Two well formed, typical chorionic villi with regular Langhans' and syncytial cells



FIG 2—Section through fallopian tube, tubo ovarian ligament and ovary (bird's eye view) (A) Cross section of tube showing absence of tubal pregnancy (B) Cystic, hemorrhagic nodule containing clotted blood. Chorionic elements such as is seen at D were present (C) Hemorrhagic nodule at surface of ovary showing chorionic villi directly below C



FIG 3—Section through another nodule in tubo ovarian ligament (A) Two well formed chorionic villi showing very regular Langhans' cell layer and loose, intact stroma and absence of hydatid mole stromal changes (B) Syncytial cells above and below B, containing regular nuclei (C) Pale decidual cells with regular nuclei

like cells with regular, uniform, round, oval or flattened vesicular or dense nuclei (whose diameter is about one and one-half to two times the diameter of a red cell) This row of cells is continuous with a layer of syncytial cells whose cytoplasmic borders are indistinct and whose cytoplasm is intensely pink and finely granular These syncytial cells are multinucleated, being composed of several vesicular or dense, well-staining regular nuclei (whose diameter is about two times that of a red cell) These syncytial cells form the bud-like blunt ends of the villus Their nuclei are regular, occasionally slightly larger, but not at all bizarre, atypical or mitotic Where the chorionic villus is seen to be in contact with the delimiting wall of the mass, the wall contains large, pale, polygonal decidual cells, with abundant clear pale cytoplasm and well staining vesicular or solid regular nuclei Their cytoplasmic borders are usually distinct and the cell aggregates have a mosaic-like appearance These decidual cells are in continuity with, and lie freely within the delimiting wall which is otherwise composed of fibroblastic and fibrous connective tissue containing numerous hyperemic blood capillaries and arterioles and showing interstitial hemorrhage and focal infiltration by round cells The outermost portion of the delimiting wall consists of the adipose tissue of the omentum The latter also shows hyperemic large blood vessels and interstitial round cell infiltration, especially perivascularly Of note is the absence of chorionic villi external to the delimiting fibrous zone and the absence of such elements from the numerous surrounding blood vessels The mosaic-like decidual reaction in some of the septa near adjacent vessels is, however, quite prominent

Several Similar Hemorrhagic Masses in Omentum These are of varying size, all being smaller than the mass described above These masses are hemorrhagic nodules with fresh and clotted extravasated blood, some contain typical chorionic villi with well-staining, regular nuclei The delimiting wall is thinner and contains an occasional larger (four times diameter of red cell) loculated nucleus such as is seen in chorionic wandering cells The chorionic nuclei show no mitoses There is definite but scantier decidual reaction or decidual cell mosaic structures The adjacent blood vessels also show marked perivascular round cell infiltration

Tube, Ovary and Tubo-ovarian Ligament (Figs 2 and 3) The small hemorrhagic areas on the surface of the ovary are devoid of a serosal covering, which is seen overlying the surface of the adjacent portion of the ovary in the form of a row of cuboidal cells These hemorrhagic nodules have the appearance of surface implants rather than intra-ovarian structures which have penetrated the surface The latter opinion, however, is not entirely excluded, as some nodules lie definitely below the surface and are covered by a portion of ovarian stroma covered by cuboidal serosal cells Within the parenchyma there are several small follicular cysts lined by a thin resting layer of regular thecal cells with scant cytoplasm and no evidence of lutein cell formation Nearby there are present granular lutein cells with polygonal cytoplasmic borders, giving the decidual-like appearance to them The fallopian tube is entirely intact The lumen is not dilated, nor does it contain blood or placental tissue The mucosal folds are regular, lined by regular columnar cells The stroma of the folds is delicate and shows no decidual reaction The muscular layer is distinct Where the tubo-ovarian ligament fuses with the tubal wall, however, the arterioles and veins are prominent About these vessels there is prominent round cell infiltration and the adjacent stroma shows edema, hyaline change and chorionic villi which lie freely within the stroma as if penetrating the latter These chorionic villi are well formed with regular nuclei and are closely situated to the hemorrhagic nodule within the ligament which contains numerous regular chorionic villi with regular nuclei The wall of this nodule is not entirely delimited and shows decidual cells Chorionic wandering cells are present but not too bizarre or mitotic Thus, all the hemorrhagic nodules contain decidual and chorionic tissue with rather regular nuclei and some chorionic wandering cells Some of the nodules are well delimited, others show penetration of the villi into the adjacent tissue Mitoses are very rare, atypism is scant Of note

is the absence of prominent solid cellular tumor-like masses such as is usually seen in chorionepitheliomatous invasion. *Pathologic Diagnosis* —(1) Multiple hemorrhagic nodules within omentum, tubo-ovarian ligament and ovary (2) Superficially implanted hemorrhagic nodules in ovary (3) These nodules contain chorionic villi and decidual tissue with rather regular nuclear structures and show chorionic wandering cells and villus penetration into adjacent tissues (4) Frank nuclear atypism, bizarreness and prominent mitoses or solid tumor-like aggression, such as is commonly seen in the usual chorionepithelioma are absent (5) The fallopian tube itself contains no decidual or chorionic tissue within it

COMMENT —From the macroscopic appearance the nodules suggested multiple (malignant) chorionepitheliomatous metastases. Histologically, however, they failed to show the typical aggressive cellular bizarreness of the usual metastasizing chorionepithelioma or hydatid mole and could possibly be interpreted as being unusual implants from an intra-abdominal pregnancy which had ruptured. The classification of this case is not as yet fully settled, as it shows border-line features. For the present, it is best classified as showing multiple chorionic tissue implants with a strong (though not purely histologic) suspicion requiring further observation by A-Z tests and clinical course to exclude the possibility of a truly malignant metastasizing chorionepithelioma.

When last seen, March 26, 1940, the patient felt well and presented an hemoglobin of 88 per cent. The uterus felt small and normal, and there was no evidence of uterine bleeding.

Discussion —In carefully reviewing the sequence of events in this case, we find a young woman who, two years previously, went through an apparently normal pregnancy, giving birth to a dead fetus. Up to three months prior to her present illness, she was free of abnormal symptoms. From that time on, she complained of vague abdominal pain. Slightly less than four weeks prior to operation she was curietted for a supposed intra-uterine pregnancy, having missed one period. Although she complained of abdominal pain on and off for three months, it was only during the 24 hours preceding operation that the pain became acute. Operation revealed a great deal of blood and many clots in the peritoneal cavity. The tubes and ovaries, particularly the right, were studded with small nodules but presented no rent indicative of a ruptured ectopic. There were a number of nodules covering the serosa of the cecum and ileum and several dark-purplish nodules varying in size from beads to small hazel nuts. A section of omentum removed for histologic study disclosed the tumors to consist of typical chorionic villi with features suggesting distinct variation from chorionepithelioma. The benignity of the lesion was more or less confirmed by the fact that four subsequent Aschheim-Zondek tests were all negative.

Two pertinent questions arise in this case. First, where was the site of the original pregnancy, was it in the tube, was it in the uterus, or was it intra-abdominal? Second, in which way does the histologic architecture of this tumor differ from that of a true chorionepithelioma?

Regarding the possibility of the uterus being the original site of preg-

nancy, all that can be stated, at present, is that, at operation, the uterus appeared and felt perfectly normal. Unfortunately, a curettage was not performed at the time of operation or immediately after to absolutely rule out this possibility. Since the lumen of the left tube was found to be apparently normal, this source can logically be eliminated as a possible site. The involved right tube and ovary, after a thorough histologic study, failed to reveal any evidence of placental tissue within the lumen of the fallopian tube. This leaves the third possibility—that the pregnancy might have been intra-abdominal. It is quite possible that the fetus might have escaped detection because of the fact that the intra-abdominal clots which were removed with moist sponges were not recovered for examination. This possibility is, however, somewhat remote since one can scarcely conceive of an intra-abdominal pregnancy being present which could, by light swabbing, be removed from its attachment.

Regarding the differential diagnosis between the case here presented and chorionepithelioma, one must fall back upon histologic and biologic criteria. A careful examination of the photomicrographs, here presented, will disclose well differentiated villi which are not commonly seen in cases of chorionepitheliomata, but which characterize normal chorionic tissue. Furthermore, the cells here seen are typical Langhans' syncytial cells with scant evidence of the nuclear mitoses, atypism or bizarreness so frequently encountered in chorionepitheliomata. In addition, one sees little evidence in any of the sections of invasion of the blood spaces by chorionic tissue which is so frequently evident in the malignant type of tumor. Taking the entire picture of the histologic structure of the tumor here presented, and comparing it with that of a typical chorionepithelioma, we are struck with a sufficient number of variants to warrant its classification among the benign rather than among the malignant tumors.

A careful review of the literature has, to date, failed to reveal an exactly similar instance of benign multiple chorionic villi intra-abdominal implantations.

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KRUKENBERG'S TUMORS*

A SURVEY OF FORTY-FOUR CASES

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KRUKENBERG,²¹ in 1896, described five cases, and a specimen of ovarian malignancy, that showed a peculiar and poorly understood gross and microscopic picture. Grossly, the tumor was of moderate size, it was nodular yet it possessed a smooth surface. Adhesions were usually absent in such cases but ascites was often found. The tumor was usually bilateral, usually solid, occasionally cystic and the general form of the normal ovary was usually maintained. The cut surface had a myxomatous appearance. Microscopically, Krukenberg described "signet-ring" cells surrounded by a fibrous stroma. He recognized the picture as one of undoubted malignancy and considered the lesion as primary in the ovaries. He classified it among the sarcomata but in the title of his thesis, "*Ueber das Fibrosarcoma Ovarii Mucocellulare (carcinomatodes)*," he obviously entertained the possibility of its origin from epithelial cells. No one has yet given a better description of this tumor than he.

Although tumors of this type now bear the name of this early investigator, historical researches reveal that he was not the only pioneer in this particular field of research.¹⁻³⁵

Important contributions were made by Waldeyer,³⁷ in 1872, and Welch,³⁸ in 1892. Knowledge of the epithelial origin and secondary nature of the lesion is due chiefly to the observations and writings of Schlagenhauser,³³ Wagner,³⁶ Glockner,¹⁵ and Romer.³⁰ Other important contributions have been made by Major,²⁵ Fallas,¹² Hundley,¹⁸ Woodall,³⁹ Jarcho,¹⁹⁻²⁰ Masson,²⁶ Shaw,³⁴ Novak and Gray,²⁸ Horsley¹⁷ and others.¹⁶

Histogenesis—Since the lesion was shown by the above mentioned writers to be secondary in most instances, all workers have agreed on this one fact. However, there is as yet no general agreement as to what constitutes a Krukenberg tumor, as to how metastasis occurs, as to whether a primary ovarian carcinoma may be impossible to distinguish from a Krukenberg

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tumor, as to whether the metastasis is in any way selective, or on how the lesion should be treated

Novak and Gray, Ewing,¹¹ and many others have expressed the belief that all or most of the original criteria set down by Krukenberg's description should be fulfilled. Jarcho, on the contrary, pointed out the great variation in the appearance of these tumors and stated that "signet-ring" cells are not always found. Most authors believe that the primary lesion, in these cases, must be a "colloid" or mucus-containing carcinoma. Novak and Gray, Jarcho, and Laison,²² however, do not agree. There is no agreement in the literature as to how metastasis occurs. Novak and Gray, Shaw,³⁴ Broders,⁹ Armstrong and Wolfe,³ Runyeon³¹ and many others have said that spread is usually by way of the lymphatic system. Others stress the possibility and probability of spread by peritoneal sedimentation. Boyd⁴ belongs to this latter school of thought. Major²⁵ reported a case in which carcinoma cells were found in the pulmonary blood vessels. This, he felt, was very suggestive that hematogenous spread occurs. That spread may occur by contiguity is probably conceded by all.

Cases of primary ovarian adeno-"colloid" carcinoma resembling microscopically Krukenberg's tumor have been reported by Schenk,³² Glockner,¹⁵ Frankl,¹⁴ Neumann,²⁷ Outerbridge,²⁹ Andrews² and others.

As to what surgical treatment should be instituted in these cases, great disagreement exists. Comando¹⁰ and others have expressed the belief that in the absence of gross generalized carcinomatosis both the primary growth and the ovaries should be removed. An opposite view is expressed by those who think that all surgery is contra-indicated. MacCarty,^{23, 24} speaking principally of primary ovarian carcinoma, has pointed out the importance of removing the uterus and tubes as well as the ovaries, to prevent recurrence in the pelvis.

Materials, Methods and Purpose of Present Study—Our material for study consists of 44 cases encountered at the Mayo Clinic from 1908 to 1938, inclusive. Five of the cases have previously been studied and reported by Masson.²⁶ Case histories were abstracted, surgical and postmortem material has been examined, and all available tissue has been studied microscopically. The presence of mucus in the primary and metastatic lesions was demonstrated by means of the Galantha stain for mucus. In 19 of the 44 cases, only surgical material and surgical records were available. In the remaining 25 cases surgical material plus complete postmortem material was available.

We wish to present our views on four important questions: (1) What is a Krukenberg tumor? (2) By what route does metastasis occur? (3) Does a primary adeno-"colloid" carcinoma of the ovary ever mimic a Krukenberg tumor? (4) What surgical procedures are indicated in dealing with these cases?

Clinical Observations—The average age of the patient when the ovarian lesion was found was 48.2 years. All except four of the patients were, or had been, married. One patient was a Negro, all the others were white persons. There was nothing typical about the case histories.

Ascites was recorded in 17 instances and absent in 27. Both ovaries were involved in 35 cases, and in nine instances unilateral involvement was found.

In 30 instances, the diagnosis of the original lesion was made first. In 14, the secondary lesion was diagnosed first, and in all but three cases the original lesion was found at celiotomy or postmortem examination. The primary lesion was found in the stomach in 20 instances, in the sigmoid or rectosigmoid in seven, in the colon in four, in the gallbladder in three, in the cecum in two, in the jejunum in two, in the uterus in one, in the breast in one, in the hepatic duct in one, and in three cases, without postmortem study, the site of the original lesion was not definitely found (Table I).

TABLE I
FINDINGS IN FORTY-FOUR CASES OF KRUKENBERG'S TUMOR

Primary Lesion		Nature of Metastatic Involvement					Average Postoperative Life (in months)
Site	Frequency	Bilateral Ovarian	Peritoneal Implant	Periaortic Nodes	Generalized Carcinoma tosis	Ascites	
Stomach	20	17	9	5	12	10	9.8
Sigmoid (rectosigmoid)	7	6	4	2	5	1	12.8
Colon	4	2	2	2	2	0	3
Gallbladder	3	3	2	1	2	2	2.5
Cecum	2	1	1	1	1	0	0.5
Jejunum	2	2	2	1	2	1	0.25
Uterus	1	0	0	0	0	0	0.75
Breast	1	1	0	1	1	0	0.5
Hepatic duct	1	0	0	1	1	0	2
Unknown	3	3	2	0	2	3	4
Totals	44	35	22	14	28	17	3.61

Pathologic Observations—Our description of the gross characteristics of the larger Krukenberg tumors that we studied would only repeat the excellent description written by Krukenberg. The largest tumor that we encountered was approximately 24 cm. in diameter, the smallest was the size of an atrophic ovary. All of the tumors that we studied had a smooth capsule, were free of adhesions, and possessed an irregular nodular contour. Associated cysts were often found. There was a striking tendency for the tumor to maintain the general form of a normal ovary. In our experience, there was not always gross evidence of other metastasis. The cut surface of the tumor had a myxomatous appearance. After a time the substance of the tumor showed a tendency to recede, leaving a concave rather than a convex cut surface. Regions of necrosis were often encountered.

Microscopically, the epithelial elements composed of large rounded or polyhedral cells were seen in groups of varying size, intimately mingled with the fibrous stroma. The epithelial cells were in some instances forming well-defined glands, in others no glandular arrangement could be seen, but rather the appearance was that of wild cellular proliferation (Fig. 1). Interestingly enough, the above variation was seen not only in different sections of the same tumor but also in different regions of the same section (Fig. 2). The nuclei of the epithelial cells were usually displaced peripherally and compressed by mucus giving rise to the "signet-ring" appearance. The fibrous

stroma varied but little, being quite dense in a few regions, but in most, loose and edematous. Little has been written regarding the stromal reaction when the ovary is invaded by a carcinoma. The loose areolar-like stroma lying between regions of dense stroma seemed to us almost constant.

COMMENT—What constitutes a so-called Krukenberg tumor? The views of others already have been given herein. With the view that all or most of the original criteria in Krukenberg's original description must be fulfilled, we whole-heartedly disagree. It is our feeling that the criteria for the

(a)

(b)

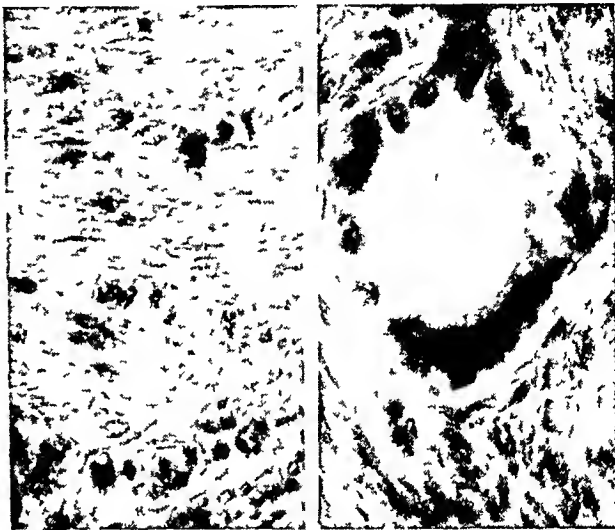
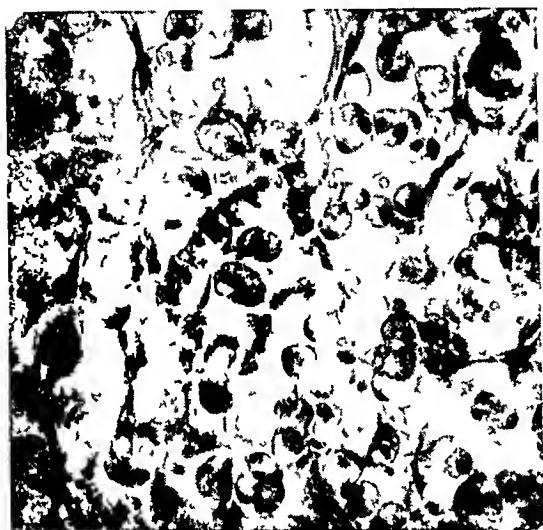


FIG 1—Typical microscopic picture of Krukenberg's tumor ($\times 275$)

FIG 2—Krukenberg's tumor, (a) section showing complete lack of differentiation, (b) section of same tumor showing glandular formation ($\times 465$)

classification of a particular pathologic finding must be such that all like lesions can be included. There is one constant finding in Krukenberg tumors and that is mucus in the epithelial cells. As previously mentioned there are those who state that "signet-ring" cells are not always found. It is true that their prominence varies greatly but in our experience careful search nearly always reveals some of them. At any rate, all will agree that mucus-containing cells are the most constant finding. All the other typical findings fail to be present in some cases. It is true that most metastatic adeno-"colloid" carcinomata of the ovary, by the time they are diagnosed, appear similar grossly and microscopically to the tumor which Krukenberg described. However, that a lesion has not had ample time to manifest a gross pathologic picture is no reason for its not being properly identified. A few metastatic "signet-ring" carcinomatous cells in the cortex or hilus of an ovary constitute a Krukenberg tumor just as does a similar tumor the size of a child's head (Fig 3). The former needs only time to mimic the latter. Ewing suggested that lesions showing acinar structures should be excluded. However, serial sections will reveal acinar structures in a high percentage of all so-called Krukenberg tumors. As previously stated it is interesting how both types of pictures can be seen in the same section (Fig 2). An ovary involved secondary to a low grade adeno-"colloid" carcinoma of the colon shows a great deal of acinar structure, yet it is not different from an ovary

involved secondary to a high grade adeno-"colloid" carcinoma of the stomach which shows a very little acinar structure. Each of these types of ovarian lesion is a metastatic adeno-"colloid" carcinoma of the ovary. We feel that these tumors should be described, like other metastatic tumors, merely as metastatic carcinoma of the ovary. Realizing, however, that the term "Krukenberg's tumor" will continue to flourish in medical literature, we contend that it should include all metastatic adenocarcinomata of the ovary. There is no real difference between metastatic adenocarcinoma of the ovary and metastatic adeno-"colloid" carcinoma of the ovary, save for the presence of mucus in the latter. However, if this difference were overlooked, not even the remotest reason would ever exist to use the term "Krukenberg's tumor."

Whether or not the presence of mucus can always be demonstrated in the primary lesion we do not know. It already has been pointed out, herein, that some workers report finding adeno-"colloid" carcinoma in the ovary secondary to a primary adenocarcinoma, which contained no mucus. This was not our observation. In every instance in which it was possible to examine the primary lesion there was definite evidence of the presence of mucus therein. The amount of mucus in the primary lesion roughly varied inversely to the grade of the carcinoma, graded by Broders'⁵⁻⁸ method on the basis of one to four.

By what route does metastasis occur? There are four possibilities that we wish to consider: (1) Spread by peritoneal sedimentation, (2) spread by lymphatic channels, which must include retrograde spread, (3) extension by continuity, and (4) spread by way of the blood stream.

Two reasons have been advanced for believing that spread may occur by means of peritoneal sedimentation: (1) Carcinoma cells are frequently found in peritoneal fluid in cases of abdominal carcinomatosis. (2) Early involvement of the ovarian cortex without involvement of the ovarian medulla is occasionally seen (Fig. 3).

Certainly no one will question the first reason. If carcinomatous cells are present in the fluid there is no reason why they should not attack the ovary just as they may and do attack other structures. What depth the primary lesion must reach in the involved wall, so that carcinoma cells may invade the peritoneal fluid we do not know.

The second reason we admit is open to question. One does occasionally encounter involvement of the ovarian surface or cortex but does not find involvement of the ovarian medulla or hilus. We have one such case (Fig. 3). By what mechanism the germinal epithelium is permeated, if it is, we do not know.

Another reason, listed by some, as previously mentioned, is the high incidence of peritoneal implants in these cases. This certainly is not evidence against the possibility of this type of spread but it must be remembered that, as Broders'⁹ has pointed out, the peritoneum contains a network of lymphatic vessels. Spread along these vessels with occasional involvement of the peritoneal surface would produce a picture similar to that described by

Boyd⁴ We do not know that this ever happens but we do know that carcinoma cells invade the peritoneal lymphatic vessels. Figure 4 illustrates a peritoneal lymphatic vessel loaded with carcinomatous cells.



FIG. 3.—Tiny metastatic nodule at periphery of ovary—one may note break in the continuity of the germinal epithelium ($\times 85$)

We feel, therefore, that since carcinomatous cells are frequently found in peritoneal fluid it is logical to conclude that metastasis by peritoneal sedimentation may occur. The occurrence of involvement of the ovarian surface, in the absence of other ovarian involvement, adds to this hypothesis. The high incidence of peritoneal implants, we feel, adds to the hypothesis but hardly justifies a conclusion either for or against it.

Factors in favor of spread by way of lymphatic vessels, some of which have been mentioned previously by others, are (1) the high incidence of bilateral ovarian involvement, (2) the smooth surface of the involved ovary, adhesions rarely being encountered, (3) maintenance by the involved ovary of the shape of the normal ovary, (4) the widespread and extra-abdominal metastasis sometimes found, (5) the high incidence of peri-aortic lymph node involvement, (6) the demonstrable evidence of carcinomatous cells in the peritoneal lymphatic vessels, and (7) the occurrence of ovarian carcinoma secondary to carcinoma of the breast.

It is obvious that no strong argument can be advanced to support the

hypothesis that bilateral involvement is suggestive of spread by way of lymphatic vessels. The smooth surface and maintenance of normal ovarian shape certainly are suggestive of growth from within. The simplest entrance to the medulla is surely through the hilus by way of lymphatic vessels (Fig 5). The widespread metastasis so often found outside the abdominal cavity necessitates spread either by lymphatic vessels or by the blood stream. It may be said that the peri-aortic nodal involvement, so often found, is secondary to the

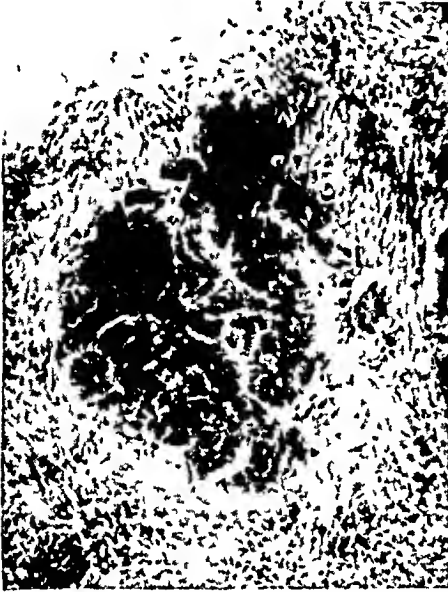


FIG 4—Peritoneal lymphatic vessel loaded with carcinomatous cells (X150)

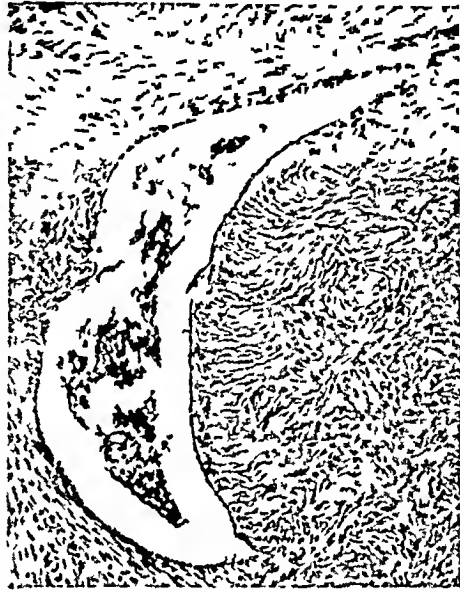


FIG 5—Cortex of ovary, showing lymphatic vessel which contains carcinomatous cells (X125)

ovarian lesion that previously had arisen by some other route. This may be true. Ovarian carcinoma secondary to carcinoma of the breast must start at least through the agency of the lymphatic or blood stream.

We believe that the above-mentioned reasons are suggestive of the likelihood of spread by way of the lymphatic vessels in many cases. As stated, this may not always be by retroperitoneal spread and in turn by retrograde spread, but may in some instances be by way of the peritoneal lymphatic vessels. Figure 6 represents a section of ovary that showed no gross evidence of metastatic lesions. By cutting several sections this tiny metastatic nodule was found. In contrast to Figure 2, showing a small nodule near the periphery, this metastatic nodule is near the medulla, adjacent to a lymphatic vessel.

Extension by continuity from structures adjacent to the ovary unquestionably does occur. Although little has been written regarding this type of spread, one may perhaps infer that it is conceded by all.

Extension by way of the blood stream certainly is within the realm of possibilities. This type of spread is sometimes used to explain metastasis from the breast to the ovary. There is no reason for thinking that blood vessels are not occasionally eroded giving rise to spread by way of the blood stream.

The only logical conclusion, with our present knowledge, is that metastasis may occur in any one or in all of the ways already mentioned. The predominant type of spread in any particular case probably depends on at least three factors: (1) The site of the primary lesion, (2) the depth to which the wall of the primarily involved viscus has been invaded, and (3) the degree or grade of malignancy of the primary lesion.

Does a primary adeno-"colloid" carcinoma of the ovary ever mimic Krukenberg's tumor? Primary adeno-"colloid" carcinoma of the ovary does



FIG 6—Hilus of ovary showing lymphatic vessel which contains carcinomatous cells ($\times 85$)

occur. The case reported by Andrews² is the most convincing, but it may yet prove to be a metastatic lesion. It may be safely concluded that primary adeno-"colloid" carcinoma of the ovary may rarely mimic Krukenberg's tumor. At present, the most plausible explanation regarding the origin in the ovary is the hypothesis that an entodermic type of epithelium predominates and inhibits the other elements in an originally teratomatous lesion.

What surgical procedures are indicated in dealing with these cases? This, of course, depends on many factors, chief of which are the patient's general condition and the extent of the growth. Given a patient who is a poor surgical risk or one showing evidence of extensive metastasis, surgical treatment is

contraindicated, save for the relief of an obstruction of the gastro-intestinal tract. Given a patient who is a good surgical risk without extensive carcinomatosis, the uterus, tubes and ovaries should be removed. This procedure is justified for three reasons: (1) The pathologist's diagnosis may be wrong, (2) the remaining days or months which the patient has to live will be more comfortable without the presence of a huge pelvic mass and abundant ascites, (3) the increased mortality and morbidity associated with this procedure are not great enough to warrant not attempting to give the patient the comfort that would result from such a procedure. Circumstances may justify leaving the uterus intact but an apparently atrophic ovary should never be left intact. Two of our cases emphasize this point. In one, a unilateral, solid ovarian tumor was removed elsewhere. This patient registered at the clinic four months later and had a tumor of the remaining ovary with considerable ascites. In the second case, which was similar to the first, not even a palliative procedure was advised owing to the extensiveness of the gastric lesion, as shown on roentgenologic examination. Both patients could have been made comfortable longer with adequate original surgical treatment. We are aware that every surgeon cannot have a pathologist at his side, particularly one who is experienced with the diagnosis of fresh tissue. A good general rule, in this case, is to remove both ovaries when a solid tumor is found involving either one, particularly if the patient is past or near the menopause.

What surgical interference is warranted in dealing with the primary lesion? This, in our opinion, usually depends upon one factor—the site of the primary lesion. All things being equal, the surgeon is justified in being more radical when the primary lesion is in the colon than when it is elsewhere, because of the frequent relatively low grade of these lesions.

Are any other types of treatment indicated? Fennel¹³ reported a case of intercurrent development of uterine carcinoma. Radium treatment for the uterine lesion was of benefit but the gastric carcinoma then seemed to become more active.

SUMMARY

We have presented 44 cases of Krukenberg's tumors, five of which previously have been studied and reported by Masson²⁶. We believe that the term "Krukenberg's tumor" should not be used. However, since, in all probability, such a term will continue to be employed, all metastatic adenocarcinomata of the ovary should be included in this group. We have attempted to show that these tumors vary only in size and degree or grade of malignancy. We have demonstrated a few metastatic, "signet-ring," carcinomatous cells in the cortex of an ovary that need only time in order to invade the entire ovary and to produce a typical gross pathologic and clinical picture of Krukenberg's tumor. We have demonstrated the tremendous structural variation seen in different parts of the same microscopic section, as evidence of the wide variation in structure throughout the tumor. This, we feel, supports our contention that tumors found to contain glandular structures when examined

microscopically should not be excluded. We have further stated that nearly all Krukenberg's tumors will show some glandular structures if serial sections are made. In our experience, mucus has always been found, as evidenced by the presence of "signet-ring" cells. The variation in the amount of glandular structure and amount of mucus, we believe, is largely dependent on the grade of malignancy of the primary lesion, varying inversely.

That metastasis may occur in one or all of four ways is our contention. This conclusion is based on the following observations. We have found peritoneal lymphatic vessels loaded with carcinomatous cells, this observation demonstrates the possibility of spread through peritoneal lymphatic channels. Peritoneal implants may arise from similarly involved, adjacent lymphatic vessels. Spread to the ovary may occur by this route. The high incidence of involvement of peri-aortic nodes is suggestive to us, as it has been to others, of spread frequently by the retroperitoneal lymphatic system. It has been pointed out that there is no reason why carcinoma may not spread by way of the blood stream, when blood vessels are eroded by the growth. We do not doubt that spread may occur by infiltration of contiguous structures. Lastly, spread by a process of peritoneal sedimentation is, to us, perfectly logical. Carcinomatous cells are frequently found in peritoneal fluid in cases of carcinoma of the stomach. Spread by this route, therefore, is logical for there is no reason why the ovary should not be involved when the peritoneum is involved, as is indicated by the presence of peritoneal implants. If one admits the logic of this argument and believes that carcinoma may spread by way of the lymph stream, blood stream, and by infiltration of contiguous structures there can be only one conclusion. That conclusion is that spread may be by any one or by all four ways.

We have stated above that the predominant type of spread in any particular case probably depends on at least three factors: (1) The site of the primary lesion, (2) the depth to which the wall of the primarily involved viscus has been invaded, and (3) the degree or grade of malignancy of the primary lesion.

It is our belief that primary adeno-"colloid" carcinoma of the ovary rarely mimics Krukenberg's tumor. Infrequently it is difficult to distinguish between an edematous primary ovarian carcinoma and a metastatic "colloid" carcinoma of the ovary. The comparatively typical stromal reaction seen in an ovary being invaded by carcinoma and its value in helping one to distinguish between a primary and secondary ovarian carcinoma has been pointed out.

It is difficult to make general rules as regards treatment. As in cases of carcinoma occurring elsewhere in the body operation perhaps offers more than does any other type of treatment. We admit, however, that we do not actually know the value of other types of treatment, particularly roentgenotherapy. We bring up the question as to whether roentgenotherapy, in some instances, may hasten death. The tendency to be more radical in dealing with this condition when the primary lesion is in the colon has been suggested because of the frequent relatively low grade of these lesions. Although

the surgeon is confronted with a hopeless situation, he must not be blinded by the futility of trying to cure metastatic carcinoma but he must realize the value of palliation and of adding a few months to the patient's life

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DESMOID TUMORS*

A CLINICAL AND PATHOLOGIC STUDY

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DESMOID TUMORS are benign fibromata arising from musculo-aponeurotic structures According to MacCarty,²⁹ they are fibrocytomata occurring in striate muscle The majority of them occur in the anterior abdominal wall, but they also occur, not infrequently, in other parts of the body

This study is concerned with the clinical and pathologic manifestations of the 77 desmoid tumors which have been diagnosed at the Mayo Clinic during the past 30 years (January 1, 1908, to December 31, 1937, inclusive) The histories of these cases have been carefully abstracted, with especial reference to sex, age, symptoms, known duration of tumor, trauma, previous operations, pregnancies, treatment and recurrence, where definite follow-up information was available The gross specimens were studied, and microscopic sections were made of each tumor in order to study cellular detail

In order to be able to compare the results of this study with the results of those reported in the literature, desmoid tumors have been divided into two groups (1) Those occurring in the anterior abdominal wall, and (2) those occurring in the musculo-aponeurotic structures elsewhere in the body

The history of desmoid tumors apparently began in 1832, with the report of two cases by Macfarlane, of Glasgow Although he did not coin the term "desmoid," there can be little doubt, from the details given, that the tumors were examples of fibroma of the abdominal wall The first was described under the title, "Organized Sarcomatous Tumour between the Layers of the Abdominal Muscles," and the other as a "Fibrocartilaginous Tumour" in the same situation The first patient was cured by excision of the tumor, the second patient died of peritonitis following excision of the tumor

Muller, in 1838, first suggested the use of the term "desmoid" because of the band and tendon-like arrangement in these fibrous tumors However, the tumors were called, and generally referred to by the French term "*fibrome de la paroi abdominale*" until Sanger (1884) revived the term "desmoid" in conjunction with his operative innovation of resecting the peritoneum in

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cases in which this membrane was adhered to the growth rather than shelling out the tumor from its false capsule as previously had been done

According to Labbé and Remy, nine cases of desmoid tumors had been reported prior to 1850. The fibrous nature and benign character of these tumors were recognized from the onset, although there was much controversy as to their point of origin. Huguier (1860) correctly stated the fibrous nature of the growth, but believed that it arose by a pedicle from the periosteum of the pelvis, and suggested section of the pedicle as a method of treatment.

While the French were being misled by Huguier, Cornils (1865) and Buntzen (1868) developed the musculo-aponeurotic theory of origin and suggested treatment by excision. Guyon, in 1877, corrected the error initiated by Huguier. In 1875, Suadicani made the great advance of applying listerism to the extirpation of these tumors.

Except for occasional case reports, the term "desmoid" was seldom seen in the literature until 1890, when Ledderhose reviewed 100 cases reported in the literature, and, in 1904, when Pfeiffer, in a monograph, collected and analyzed 400 cases (40 of his own and 360 reported in the literature). Since then various case reports and summaries have appeared in the literature, such as those of Stone, Balfour, Stewart and Mouat, Bessesen, Bevan, Cullen, Delbet, Marlow, Polacco, Powers, Walters and Church, Nichols, Danforth, Cahn, Andrews, Mason, Penick, and Geschickter and Lewis.

Mankin collected, from the literature, reports of 629 cases of neoplasms of the anterior abdominal wall, in 423 of the cases the neoplasm was a fibroma and in 152 it was a fibrosarcoma.

Most of the reports have concerned desmoid tumors of the abdominal wall, however, in a number of cases of desmoid tumors, such as those reported by Bellanger, Cigolini, Salto, Auvray,^{2, 3} Hoffmeister, Mason and Esau, the tumors occurred elsewhere in the musculo-aponeurotic structures of the body.

Desmoid tumors are of comparatively infrequent occurrence. Gurlt, of Vienna, found only eight in a study of 16,637 tumors. Labbé and Remy observed ten cases during 20 years, Billroth, 16 in 23 years, Nélaton, 15 in 26 years, Pfeiffer, 40 cases at von Brun's Clinic, at Tübingen, in 46 years, and Mason, 50 cases during 24 years.

Although the real cause of these tumors still remains unknown, much has been written on this phase of the subject.

In the 400 cases included in the monograph by Pfeiffer, 87.1 per cent of the patients were women. Data regarding the occurrence of pregnancy were available in 265 of the cases in which the patients were women. In 250, or 94.3 per cent of the 265 cases, the patients had borne children. In 93 per cent of the cases reported by Stewart and Mouat the patients were women, and 80 per cent of these women had borne one or more children. In most of the cases reported by Stewart and Mouat the tumor occurred in the third or fourth decade of life. Geschickter and Lewis reported 20 cases of desmoid tumors of the abdominal wall. In 19 of the cases the patients were females, in 17 of the 19 cases the patients were between the age of puberty and the

menopause All of the tumors were related to pregnancy or the scar of an operation These authors stated "The rarity of such fibromata is in keeping with the simple and direct formation of adult fibrous tissue from mesenchyme The simplicity of this differentiation in a tissue which retains its power of regeneration supplies very few 'embryonic tests,' in the sense of Cohnheim, from which tumors might arise" These authors expressed the opinion that there is some relationship between these growths and sex physiology

Stewart and Mouat said that there was a history of trauma or severe muscular strain in nine of their cases and that the tumor occurred in an operative scar in five cases Penick, in a review of the literature, found reports of 15 cases in which the tumor arose in operative scars and added two cases in which this occurred Auvray,² Esau Hoffmeister, and Cigolini also reported trauma as a possible causal factor Ebner, in 1880, advanced the theory now held by MacCarthy,²⁶ namely, that these tumors result from muscular rupture either in consequence of violent effort or traumatism Labbe and Remy (1888) suggested that muscular rupture during violent contractions of labor was the real explanation, that is, the physiologic trauma of labor

In view of the traumatic theory, Nørgaard contrasted the comparatively common hematoma of the rectus muscle caused by severe strains or infectious diseases with the rare spontaneous hematoma in the same muscle In all of the 72 cases which he reported, the patients were women, and all of the women except one were multiparae In 11 cases spontaneous hematoma occurred during pregnancy The clinical picture was usually misinterpreted and practically all of the patients were treated surgically

It appears highly probable that this condition may be the basis of desmoid tumors, that is, organization in an hematoma and subsequent hyperplasia, the cause of the latter being unknown Repetto expressed the opinion that a desmoid tumor is the result of an inflammatory reaction in a small hemorrhage in the abdominal wall followed by fibrosis and hyperplasia

Various clinical observations have been reported in regard to these tumors Stewart and Mouat said that the tumor is usually discovered accidentally by the patient or by a physician after some slight trauma has led to physical examination The presence of the tumor may occasionally cause pain of a localized or radiating nature Even when the tumor has attained considerable size it rarely causes pressure symptoms, and signs and symptoms of intra-abdominal involvement are lacking The tumor does not involve the skin, which can be moved freely over the tumor With the abdominal muscles relaxed, the tumor can be moved about in certain directions with sufficient freedom to show that it is unconnected with any intraperitoneal structure It is also immobilized by contraction of the muscle or muscles in which it lies and recovers its mobility when the muscles are relaxed It must be considered in the differential diagnosis of tumors occurring in operative scars, as pointed out by Balfour, Danforth and Mason Cigolini, Salto, Auvray^{2, 3} and Esau have pointed out that the tumor must be suspected in all cases in which a

tumor occurs in muscle and that a biopsy should be performed to determine its exact nature

The gross and microscopic appearance has been well-described by various authors. Stewart and Mouat reported that the tumors always occur singly. They may be oval, round or flat, and they may vary in size from 1 to 12 cm in diameter. Rokitsky (1880) described one weighing 17 Kg. Montgomery and Bland (1905) reported a case in which the tumor weighed 19 pounds (8.6 Kg). The tumor may become adherent to the fascia or peritoneum. Owing to the pressure of the growing tumor against adjacent structures it may appear encapsulated. It is densely hard, white or pinkish, and cuts with difficulty.

The microscopic structure, according to Geschickter and Lewis, is that of a rather cellular fibroma occurring in striate muscle. The tumor is clearly an infiltrating type, without a capsule. The especial features of the tumor are the inclusion of striate muscle, as described by Durante (1902).

The treatment, according to most of the writers on the subject (Balfour, Mason, Stewart and Mouat, Pfeiffer, Penick, and Geschickter and Lewis), is surgical.

The prognosis, according to Geschickter and Lewis (1935), is good, as the majority of their patients lived well beyond the five-year period, after surgical removal of the tumor. Pfeiffer (1904) in a postoperative study of 107 cases found a recurrence in 33, or 30.8 per cent. In Stone's first case (1908) the tumor recurred and was again excised, 20 years after the first operation. In Morison and Drummond's case there was no evidence of recurrence two years after the second excision.

ANALYSIS OF CASES

An analysis of the present series of 77 cases of desmoid tumor reveals that in 55 cases the tumor occurred in the anterior abdominal wall, and in 22 cases it occurred elsewhere in the skeletal muscular system (Table I).

TABLE I
SITE OF DESMOID TUMORS

Site of Tumor	No. of Cases
Anterior abdominal wall (rectus abdominis, external or internal oblique or transversalis muscles)	55
Pectoralis major	5
Muscles about the scapula	4
Rectus femoris	3
Gluteal muscles	2
Sternomastoid muscle	1
Posterior belly of digastric muscle	1
Biceps brachii	1
Extensor carpi ulnaris	1
Hamstring muscles (biceps femoris, semitendinosus and semimembranosus)	1
Dorsum of foot	1
Masseter	1
Scar of radical operation on the breast	1
Total	77

The following is an analysis of the 55 cases in which the tumors occurred in the anterior abdominal wall. In 40 cases, the patients were females, and in 15 cases, the patients were males. Most of the tumors occurred between the ages of 20 and 40, among the females, and between 40 and 60, among the males. The size of the tumors varied widely, in most cases the tumors were between 3 and 8 cm in diameter. The known duration of the tumors varied from one month to several years. No relationship was noted between the size of the tumor and its known duration. There was a history of pregnancy in 25 of the 40 cases in which the patients were females. A history of trauma was obtained in four cases, and in 14 cases the desmoid tumor occurred in an operative scar. In 47 cases the patients were treated by excision, and in eight cases they were treated by a combination of excision and irradiation. Follow-up information was available in 47 of the cases in which the tumor occurred in the anterior abdominal wall. In 39 of the 47 cases excision only was employed, and in the remaining eight cases excision and subsequent irradiation were employed. Local recurrence of the tumor was noted in three cases in which the treatment consisted only of excision of the tumor, and in one case in which irradiation was employed following excision. In two of the three cases in which a local recurrence followed treatment by excision only, the recurrent tumors were excised, and follow-up data are available for eight and ten years, respectively, after the second operation. The tumor did not recur after the second operation in either case. In the 55 cases in which the tumors involved the anterior abdominal wall, 20 patients were known to be alive ten years, and 16 patients are known to be alive five years, respectively, following the completion of treatment. There were 20 known ten-year cures and 16 known five-year cures in this group of cases.

The following is an analysis of the 22 cases in which the tumor occurred elsewhere in the skeletal muscular system than in the anterior abdominal wall. The site of the tumors is shown in Table I. In the 22 cases, seven patients were males and 15 were females. Most of the tumors occurred between the ages of 20 and 40, in the females, and 40 and 60, in the males. The size of the tumors varied from 1 cm to 10 cm in diameter. The known duration of the tumors varied from one month to 24 years. No relationship was noted between the size and known duration of the tumor. There was a history of pregnancy in eight cases, and a history of trauma was obtained in two cases. The tumor occurred in an old operative scar in only one case (Table II). In 16 cases, the patients were treated by excision only, and in six cases, the patients were treated by excision combined with irradiation therapy. Follow-up information was available in 15 cases. In ten of the 15 cases, treatment consisted of excision only, in the remaining five cases, excision was followed by irradiation. There was a local recurrence of the tumor in the ten cases in which excision only was employed, but no local recurrence was observed in the five cases in which excision was followed by irradiation. In the 22 cases, in which the tumors were situated elsewhere than in the anterior abdominal wall, three of the patients have lived for ten years, and four patients

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have lived for five years, respectively, following the completion of treatment (Table II)

TABLE II
CLINICAL DATA AND RESULTS OF TREATMENT IN 77 CASES OF DESMOID TUMOR

Site of Tumor	Sex		History of Pregnancy	History of Trauma	Tumors Occurred in Operative Scar	Treatment		Results					
								Patients Known to have Lived 10 Years Following Treatment		Patients Known to have Lived 5 Years Following Treatment		Recurrence of Tumor	
	Males	Females				Excision Only	Excision and Irradiation	In Cases in which Excision Only was Employed	In Cases in which Excision and Irradiation were Employed	In Cases in which Excision Only was Employed	In Cases in which Excision and Irradiation were Employed	In Cases in which Excision Only was Employed	In Cases in which Excision and Irradiation were Employed
Anterior abdominal wall	15	40	25	4	14	47	8	18	2	12	4	3*	1
Other parts of body	7	15	8	2	1	16	6	1	2	2	2	3	—
Total	22	55	33	6	15	63	14	19	4	14	6	6	1

* In two of these cases the recurrent tumor was excised, in the two cases there was no evidence of a second recurrence eight and 12 years respectively after the second excision

The following is an analysis of the 77 cases Twenty-two of the patients were males and 55 were females A history of pregnancy was obtained in 33 cases, a history of trauma was obtained in six cases, and the tumor occurred in an operative scar in 15 cases In 63 cases, treatment consisted of excision only, in the remaining 14 cases, excision was followed by irradiation There was a local recurrence of the tumor in six, or 9.5 per cent, of the 63 cases in which excision only was employed, and in one, or 7.1 per cent, of the 14 cases in which excision was followed by irradiation There were 23 known ten-year cures and 20 known five-year cures

There was only one postoperative death in the entire series of 77 cases This was due to infection of the operative incision following the removal of a large desmoid tumor from the anterior abdominal wall (an operative mortality of 1.3 per cent)

CLINICAL ASPECTS

Desmoid tumors must be considered in the differential diagnosis of all masses that are situated in or come in contact with the musculo-aponeurotic structures of the body In this series of cases the patients, generally, sought aid because of the presence of a tumor mass Other less frequent complaints were A dragging sensation or sense of weight in the abdomen, a mild sticking pain, a sudden increase in size of a previously small nodule, a bizarre pain in the abdomen, and a sense of pressure on the bladder

In this series of cases the desmoid tumors were found more frequently in the anterior abdominal wall than elsewhere in the body and, occasionally, had

been diagnosed by the clinician as being intra-abdominal. They had been mistaken for hydrops of the gallbladder, a large stone in the gallbladder, a tumor of the omentum or mesentery, pancreatic cyst, a uterine tumor, a tumor of bone, and a tumor of kidney. When situated elsewhere in the body they generally had been mistaken for sarcomata.

The following points have proved of value in the clinical diagnosis of these tumors. As a rule the tumor is smooth, round or flat, firm and discrete. The tumor is situated below the skin but is not attached to it. The tumor is movable, moves with the muscle to which it is attached, and is immobilized by contraction of this muscle. On deep inspiration the tumor moves forward but not downward as do most intra-abdominal tumors.

A desmoid tumor must be distinguished from keloids, fibrosarcomata, inflammatory conditions, and lesions which extend secondarily to the abdominal wall from nearby organs. A keloid will, more frequently, be difficult to distinguish from a desmoid tumor than will other conditions mentioned because this overgrowth of fibrous tissue is closely allied to the desmoid tumor and resembles it in many respects. The common keloid involves the skin and subcutaneous tissues to form raised regions covered with shiny epithelium, in this respect it differs from a desmoid tumor, which involves the skin occasionally, and then only secondarily, and is usually situated below the skin. These two conditions can also be differentiated microscopically. The keloid is relatively acellular with conspicuous tracts of collagen, the remains of obliterated capillaries are usually visible. A desmoid tumor is more vascular and more cellular than a keloid and evidences of cellular activity are more noticeable.

According to MacCarty,^{27 28} the only way to be certain of the diagnosis is to remove a specimen at the time of operation and examine it microscopically.

GROSS AND MICROSCOPIC PATHOLOGY

A freshly removed tumor is dense, hard and tough, and creaks under the knife. The cut surface bulges, is white or pinkish in color, glistens, and the interlacing bundles of white fibrous tissue are usually seen without difficulty (Fig. 1). The larger tumors tend to be soft in the center, either from edema or mucoid degeneration, and some are cystic. Changes in the skin covering the tumor are unusual. There was no associated involvement of the lymph nodes in this series of cases.

The histologic picture is that of a rather cellular fibroma occurring in striate muscle. The central portion of the tumor proved to be older than the peripheral portion. The elongated adult fibrous tissue cells run in strands and bundles which are interlaced in all directions after the manner of the unstriate muscle bundles in a uterine fibroid (Figs. 2 and 3).

At the periphery, where the tumor infiltrates the surrounding muscle, there is a tendency for the tumor to be somewhat more cellular. There is no capsule or definite line of cleavage between the tumor and the adjacent muscle. It is only when the tumor is bounded by a fascial plane that the appearance of

encapsulation is produced (Fig 4) In spite of this infiltration there was no evidence of a sarcomatous change, such as nuclei containing large amounts of darkly-stained chromatin or large multiple nucleoli, both of which are indications of rapid proliferation Normal adult blood vessels were noted throughout most of the tumors These vessels were an indication of the slow growth of the tumor



FIG 1

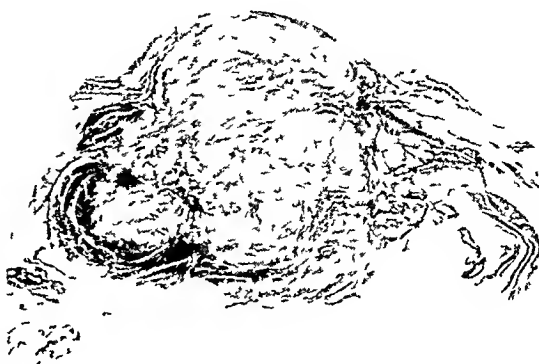


FIG 4



FIG 2



FIG 5

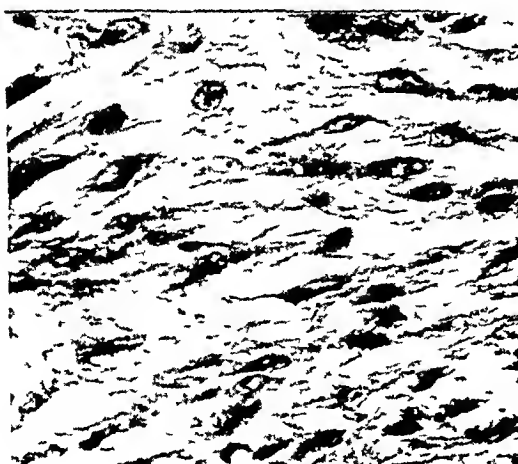


FIG 3

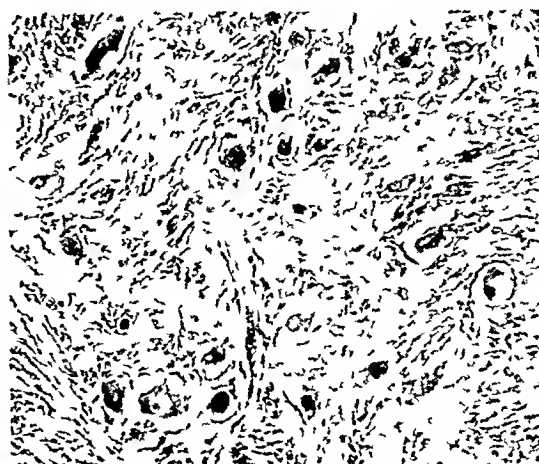


FIG 6

- FIG 1—Desmoid tumor removed from abdominal wall, showing the characteristic band like arrangement
FIG 2—Cellular character of desmoid tumor ($\times 285$)
FIG 3—Cellular but benign appearance of a desmoid tumor ($\times 450$)
FIG 4—Cross section of tumor lying between separated fibers of the rectus abdominis muscle in the rectus sheath, the tumor appears to be encapsulated ($\times 134$)
FIG 5—Infiltration of muscle fibers by a desmoid tumor ($\times 30$)
FIG 6—Muscle with "foreign body like" giant cells ($\times 195$)

The special features of the tumor were the inclusion of striate muscle fibers and the sequence of regressive changes. The earliest change was seen at the periphery of the tumor where the striate muscle was being infiltrated and broken up into constituent fibers (Fig 5).

The muscle fibers appeared to be stretched and attenuated. They were irregular in outline and the transverse striations tended to disappear. Here and there were strands resembling unstriate muscle and "foreign body-like" giant cells derived from this muscle probably because of faulty nutrition (Fig 6).

It is easy to see that failure on the part of the surgeon to remove the tumor completely would leave strands of interfibrillar desmoid tissue and result in a local recurrence of the tumor.

COMMENT—The cause of these tumors as yet remains unknown. However, the most logical theory of origin seems to be one of trauma superimposed on individual predisposition. A history of trauma was obtained in 21 cases (accidental trauma in six cases and operative trauma in 15 cases), and a history of pregnancy (physiologic trauma of labor) was obtained in 25 cases. Thus trauma appeared to be an etiologic factor in 46, or 60 per cent, of the cases studied. The endocrine theory, as related to pregnancy, seems void because 22 patients were males and only 33 of the 55 females had been pregnant.

No differences in etiology, clinical findings, pathology, curative treatment, or prognosis could be noted between the tumors which occurred in the anterior abdominal wall and those which occurred in other parts of the body.

At first glance, it would appear that a combination of excision and roentgenotherapy would be the ideal treatment, since there was a recurrence in 9.5 per cent of the cases in which the patients were treated by excision only, and in only one, or 7.1 per cent, of the cases in which the patients were treated by a combination of roentgenotherapy and excision. However, several factors have to be considered: (1) The small number of cases in which the patients were treated by excision and radiation (14) as compared to the number treated by excision only (63), (Table II), (2) the insignificance of the difference in number of five-year and ten-year cures obtained by the two methods (Table II), (3) no definite criteria were used for the employment of roentgenotherapy—it was employed in some cases in which the tumor was completely removed surgically but was not used in some cases in which the tumor was large or difficult to remove, and (4) a few of the patients had been treated unsuccessfully by roentgenotherapy only before they finally were cured by surgical treatment.

SUMMARY

This paper is based on a study of 77 cases of desmoid tumors. In 55 cases the tumor occurred in the striate muscle of the anterior abdominal wall, and in the other 22 cases it occurred in striate muscle elsewhere in the body. A desmoid tumor is a simple fibrous tumor that arises in musculo-aponeurotic

structures and tends to infiltrate the muscle in which it lies. Trauma (accidental, operative, or the physiologic trauma of labor) combined with an unknown individual predisposing factor, appears to be the most logical theory of origin. There was a peculiar change in the striate muscle fibers enclosed in the growth. This change appears to be a process of differentiation and results in the formation of multinucleated plasmodial masses resembling foreign body giant cells. These tumors do not undergo metastasis nor do they endanger life, however, they do tend to recur locally, unless completely removed. Diagnosis is made by finding a fibrous tumor in muscle, the tumor is fixed by contraction of that muscle. A biopsy is indispensable for diagnosis. Treatment consists of complete excision. Roentgenotherapy appears to be of little, if any, additional value. The operative mortality in this series of cases was 1.3 per cent. There was a local recurrence of the tumor in seven, or 11.8 per cent, of the 69 cases in which follow-up data were available. We did not discover any evidence that this tumor ever undergoes sarcomatous change.

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TECHNIC OF TATTOOING WITH MERCURY SULFIDE FOR PRURITUS ANI

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IN A BRIEF REVIEW of the history of tattooing employed in surgery, Shie¹ stated that, in 1835, Pauli had successfully employed tattooing with mercury sulfide and white lead for the restoration of the natural color to the skin in cases of *nevus maternus* and superficial *nevus vascularis*, that Schule, in 1850, had recommended cosmetic tattooing with mercury sulfide following plastic operations upon the lips, and that the natives of Africa had incorporated powdered carbon in the wounds of other parts of the body so that the healed scar would be black to match the color of their skin. Carton,² in 1909, described the use of tattooing by the native savages of North Africa for the treatment of a variety of other lesions including the neuralgias. The association of tattooing therapy with neural lesions has more than passing significance. Dohi,³ in 1909, noted that syphilitic cutaneous lesions do not appear in the areas tattooed with mercury sulfide. Dohi's observations had been confirmed by Aoki⁴ and Belote.⁵ On the basis of these observations, Cattani,⁶ in 1922, recommended therapeutic tattooing with mercury sulfide (and other drugs usually employed topically) for the treatment of chronic, localized cutaneous lesions. In 1938, Hollander⁷ reported his studies on tattooing with mercury sulfide for the successful treatment of intractable pruritus ani.

While a critical attitude toward a newly proposed treatment for pruritus ani is justified (since over 200 different forms of treatment are said to have been proposed⁸), the distressing character of the lesion warrants the trial of new procedures. It is with such an attitude that we approached the investigation of the treatment of pruritus ani by tattooing with mercury sulfide. For this study, 22 patients with intractable pruritus ani of long standing, who had failed to respond to established therapeutic measures, were accepted for tattooing with mercury sulfide. The results obtained in this group of patients was so satisfactory as to encourage the continuation of tattooing with mercury sulfide as a therapeutic procedure.⁹ On the basis of subsequent experience, one of us (R T) has extended this form of treatment to a wider variety of cases.^{10, 11}

The mechanism of the action of mercury sulfide deposited in the corium by tattoo is still undetermined. Our control studies showed that the me-

chanical trauma, alone, as produced by the tattooing machine without the employment of mercury sulfide is ineffectual in controlling pruritus and permanently.⁹ The present investigations suggest that a pharmacodynamic degenerative effect upon the cutaneous terminal nerve supply is produced which alters the capacity of the terminal nerve network to respond to adequate stimuli.¹⁰ It is, also, likely that the alteration in the cutaneous modalities is proportional, within limits, to the amount of the intracutaneous deposit of mercury sulfide.^{10, 12} These problems are new and are receiving further study.

Cattani⁶ felt that mercury sulfide deposited in the corium may act as an antiseptic. However, convincing proof for this contention is still lacking. Dohi,³ long ago, questioned the value of mercury sulfide in infections other than syphilis.

The studies of the effect of the intracutaneous deposit of mercury sulfide by tattoo upon the activity of the cells of the reticulo-endothelial system (which are present in abundance in the corium) are being pursued.

In this communication the technic of therapeutic tattooing of the anal canal and perianal circumference will be described in detail. Since the adoption of this technic the incidence of "skipped" areas (where localized areas of pruritus may continue, and which is erroneously regarded as a recurrence of pruritus) has been greatly eliminated.

Surgical Anatomy of the Anal Canal—Embryologically, the anal canal begins at the pectinate line or the level of the papillae and crypts of Morgagni. For practical purposes¹³ the starting point of the anal canal can be considered as the level at which the rectum passes through the pelvic diaphragm, *i e.*, where the so-called fibromuscular anorectal ring is formed by the internal sphincter, the deepest portion of the external sphincter, the puborectalis portion of the levator ani muscle, and by the longitudinal muscles of the rectum. The epithelium above the pectinate line is cuboidal and columnar in type. The epithelium of the anal canal between the pectinate line and the anal intermuscular septum (the point of attachment of the longitudinal muscle of the rectum to the lining of the anal canal between the lower border of the internal sphincter and the upper border of the subcutaneous portion of the external sphincter muscle) is firmly adherent to the underlying tissues, and consists of a modified squamous epithelium possessing no sweat and sebaceous glands, nor hair follicles. Below the level of the anal intermuscular septum, there is true skin which covers the anal and inferior aspects of the subcutaneous component of the external sphincter muscle. In pruritus ani, variable portions of the modified skin of the anal canal and of the true skin of the perianal circumference are involved.

The sensory nerve supply of the lining of the anal canal is primarily derived from the filaments of the inferior hemorrhoidal nerve.

General Procedure—Systemic and general dermatologic disease having local anal and perianal representation are always appropriately treated and eliminated, if possible, prior to tattooing. When, however, the underlying

disease cannot be identified and successfully eliminated, one is forced to treat the symptom

Women with pruritis ani and perinei, which occurs at or past menopause, are given a trial of estrogenic therapy (the equivalent of 150,000 to 250,000 iat units of estradiol benzoate* (Progynon B) administered in bi-weekly, intramuscular doses of 10,000 R U). If the localized pruritus is unrelieved following endocrine therapy, tattooing with mercury sulfide is carried out

Prior to tattooing, the patient is patch-tested for evidence of cutaneous sensitivity to mercury, using 2 to 5 per cent ammoniated mercury ointment. Positive reactors should not be tattooed with mercury or its derivatives.

Tattooing with mercury sulfide or other chemicals is never carried out in the presence of inflammatory and infectious disease of the preformed anal ducts, anal glands, and the crypts of Morgagni. Lesions such as anal ulcers, hypertrophied papillae, suppurations, fistulae, and hemorrhoids, which are the result of infection of the previously mentioned anal structures, are always eradicated prior to tattooing. Redundant perianal skin, even in the absence of anal lesions, is excised to facilitate tattooing.

Operation and tattooing are never performed at one sitting because the primary operation may be adequate for the control of pruritus. Secondly, in the presence of open wounds, the mercury sulfide may get into the subcutaneous tissues and form mercury protemate, which is toxic.

Armamentarium—The armamentarium consists of an electric tattooing machine,† such as that used for ornamental tattooing, with needle handles containing eight to 20 needles in a single row (in a tubular metal sheath), and protruding for 2 to 4 mm from the end of the sheath. The tubular sheath is adjusted so that when the machine is at a standstill the needle points are flush with the end of the sheath.

During tattooing, the needles have an up-and-down movement (the amplitude of which is 2 to 4 mm) and a speed of about 3,000 vibrations per minute. A technical knowledge of the component parts of the machine, such as the terminals, the switchboard, the footswitch, and the rheostat is essential, and can be mastered best by actual contact with the equipment. The needle handles and the sheath are sterilized by boiling in water or preferably by formaldehyde vapor.

Technic—The therapeutic tattooing of the anal and perianal regions requires from 45 to 60 minutes and is preferably undertaken in a hospital. In most cases, satisfactory tattooing is accomplished in one sitting.

The choice of an anesthetic depends on personal experience and preference. Any form of anesthesia that will last for an hour or longer is satisfactory. From a practical standpoint, the oil-soluble anesthetics (which alone have been employed for the treatment of certain cases of pruritis ani)

* Supplied by Dr. W. H. Stoner, The Schering Corporation.

† Recently, one of us (R. T.) has developed a simple, reciprocating, pneumatic tattooing pistol which has many advantages over the instruments employed previously.

are desirable. However, in order to permit a critical evaluation of the therapeutic tattooing alone, we have purposely refrained from using the long-acting oil-soluble local anesthetics because their inclusion would be equivalent to employing two forms of therapy.

The field to be tattooed is prepared as for any other anorectal surgical procedure. For practical reasons alcohol and ether are used rather than colored skin antiseptics. Following alcohol-ether preparation, it is customary to rub phenolized petrolatum into the skin which is to be tattooed.

The mercury sulfide is made into a moderately thick paste by mixing it with sterile distilled water. The end of the tubular sheath of the tattooing machine is either dipped into the paste or part of the paste is deposited in a specially constructed tip. The vibrations of the machine cause the paste to escape slowly to the points of the needles and thus the medication is deposited intracutaneously.

The tubular sheath of the machine should be held at an angle of about 40° to the skin. The skin should be held taut to obliterate the anal and perianal folds and to facilitate the penetration of the needles and the chemical into the corium. An area of skin, one centimeter long, the width of which varies with the number of needles used, is tattooed at a time. A slow,* steady, forward and backward or rotary motion of the instrument with light pressure against the skin is employed. This maneuver is repeated several times in the same area until the skin shows a uniform and permanent red stain which is evidence that a sufficient supply of mercury sulfide has been deposited in the corium. Adjacent skin is similarly treated until the entire pruritic region is tattooed.

The skin of the anal canal is treated first. Tattooing is begun at the anal verge and is carried cephalad to the pectinate line, using the needle handles containing 15 to 20 needles. The perianal skin is then tattooed radially to the anal orifice, beginning about one centimeter beyond the natural line of demarcation of the area of pruritus, which is discernible in the majority of cases. In the absence of such natural demarcation, it is desirable to delineate the extent of the involved perianal skin before the anesthetic is administered.

During the process of tattooing some of the paste of mercury sulfide escapes from the instrument and stains the untreated skin. It is essential to eliminate this excess paste by frequent wiping of the treated and untreated skin with gauze in order to avoid missing small areas of skin where localized areas of pruritus may continue. By tattooing the anal canal before the perianal region, staining of the lining of the anal canal with red mercury sulfide coming from the perianal circumference has been avoided. In spite of these measures, it is at times impossible to avoid skipping small areas of involved skin. These can, however, be dealt with easily at a subsequent time, if necessary.

* The speed of tattooing has been increased considerably with the use of the new pneumatic pistol.

After the completion of the tattooing, the treated area is covered with either phenolized petrolatum or with an ointment containing an anesthetic, such as ethyl aminobenzoate, metycaine or pontocaine. Edema and tenderness may occur and persist for 24 to 48 hours or longer, and are relieved by the application of anesthetic ointments, witch hazel dressings, hot compresses or by hot hip baths.

Desquamation of the tattooed epidermis ensues within a few days and reepithelization usually takes place in a few weeks after tattooing. Therefore, the mercury sulfide, to be effective, must be deposited in the corium. Deleterious effects or a foreign body giant cell reaction (commonly seen after the intracutaneous introduction of other foreign bodies) have not been observed in a comprehensive clinical and histologic study of skin tattooed with mercury sulfide.¹²

SUMMARY

A detailed description of the technic of tattooing with mercury sulfide for the treatment of intractable pruritus ani is presented.

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VARICOSE VEINS

AN ANALYSIS OF THE RESULTS OF VARIOUS OPERATIVE PROCEDURES

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DURING recent years there has been an increased interest in the treatment of varicose veins. This is evidenced by the number of publications on the subject as well as by the diversity of suggested methods of attacking this problem. However, very little that is new, either as regards treatment or mechanism of the disturbance has been brought forth.

In reviewing the many papers on varicose veins, we fail to find satisfactory follow-up studies of the patients treated, which makes it difficult to arrive at a comparison of end-results. Most writers have stressed one or another form of treatment without giving the end-results of their therapy. In no instance have we found the end-results compared, when various methods of treatment have been employed in the same clinic.

It is our purpose to present an analysis of the results of operative procedures in 121 patients cared for in the Varicose Vein Clinic of the New York Hospital, during the six years from 1932 to 1938.

Ochsner and Mahorner¹ have recently given an excellent and detailed account of the history of the treatment of varicose veins, therefore, no reference will be made to historical data here.

The forms of treatment of varicose veins most commonly employed at present are the following:

Injection—At present, the most popular treatment of varicose veins is the injection of various sclerosing substances, of which sodium morrhuate is probably the most widely employed. Recurrences following injection are reported variously from zero to 98 per cent. Steubner,² in reporting 104 cases with 158 extremities completely treated by injection, was able to state that there had been no recurrences during a 15-month period. It is not stated how long the patients were followed after treatment. DeTakats³ reports 106 per cent recurrences in 389 cases injected, but fails to tell the length of the follow-up studies. Howard, Jackson and Mahon,⁴ however, report 98 per cent recurrences in 49 patients one year or more after treatment. They stress recanalization as a natural response to thrombosis and rightly state that treatment by injection—unaided by ligature, excision or stripping of main venous channels and perforating veins—will not assure a permanent cure in cases of varicose veins, except in a few isolated cases of dilated single veins with competent saphenous and perforating veins.

Simple Ligation—Trendelenburg⁵ advocated ligation of the varicose veins in the mid thigh, and his results have been presented by Perthes,⁶ showing 22 per cent recurrences in from five months to nine years. Although subsequent authorities are in agreement that this is a poor procedure and gives rise to a high incidence of recurrences, it is carried out in a large number of cases. DeTakats³ reports 50 cases in which ligation was performed below the proximal competent vein. There is no mention made of tying off collateral vessels. No deaths followed this procedure, but three infected wounds are reported. While the follow-up on these patients is vague, all were said to be free from recurrences if the operative indications were correct.

Simple High Ligation—High ligation preliminary to injection of sclerosing solutions has been employed extensively, many preferring to use it as an ambulatory treatment. Fergusson⁷ reports 226 ligations upon 178 patients, with no deaths, and three infected wounds. The site of ligation is not clearly indicated but probably was high. His three- and four-year results include 37 operations upon 26 patients, with no relief of symptoms in two, venous stasis in six, and enlarged veins in 14. Eight of the patients with enlarged veins have no symptoms. In the classification employed in our follow-up, 14, or 35 per cent, of these results would be considered poor.

DeTakats and Quillen have carried out 200 ambulatory operations and stress the value of high ligation. The absence of pulmonary emboli is particularly noted, whereas little attention is given to hemorrhage, hematoma, infection of the wound with formation of an abscess, of an infection with death from septicemia, and reaction to procain which are present in the list of complications recorded. No injection was made at the time of operation because the majority of patients developed thrombosis without injection. Of the 200 cases, only 60 private patients were followed, and the length of the follow-up is not mentioned in these save in one followed for four years. They report dilatation proximal to the ligation in five, and distal to it in two cases.

Edwards⁸ reviews the anatomic factors in high ligation of the saphenous vein, and recommends this procedure followed by injection, but he reports no follow-up studies.

High Ligation and Injection—In the group of cases treated by high ligation and injection, follow-up studies are given with greater frequency than in the preceding methods. Lowenburg⁹ used this treatment in 49 instances and reported 89 per cent cures, 4 per cent with fair results, and 7 per cent with recurrences. The length of the follow-up in his cases is not stated. Faxon and Barlow¹⁰ have used high ligation and injection as an adjunct to injection alone in 1,072 extremities. Their end-results are based upon 365 operations performed upon 228 patients followed from 18 months to five years, with an average follow-up of 2.9 years. They record perfect results in 55 per cent, or 200 extremities; this estimate of results is made upon complete relief of symptoms and absence of tension in any of the veins left. Satisfactory results were present in 25 per cent, or 90 extremities. In this group are patients who are symptomless but have definite varicose veins.

The authors classify 20 per cent, or 75 extremities, as failures. In these patients the veins are again present with stagnation of blood in the superficial system. The presence of a recurrent ulcer placed the results in a category of failures. Retrograde injection of the distal segment in 90 per cent of the cases at the time of operation made no difference in the final rating. As complications, they list infected wounds in 2 per cent of their patients, and three cases of pulmonary emboli, of which two were fatal. In one case the femoral vein was ligated and injected by mistake. Their failures are attributed to faulty technic. In 29 extremities a high ligation was not performed, and in 35 extremities incompetent communicating veins were present.

Howard,¹¹ in 91 ligations and injections, was able to examine 78 a year or more after treatment. He demonstrated recanalization in 100 per cent but considered 77 per cent cured, as they had no visible dilated veins, in 15 per cent, the symptoms remained or recurred. The complications include hemorrhage in one case followed by a pulmonary embolus. These cases were followed from one year to 29 months.

High Ligation and Excision—Linton,¹² in 50 cases, has divided the perforators beneath the fascia of the lower leg in addition to a high ligation, but he mentions no follow-up on his cases. This procedure presents the same problem as the older extensive operations of Madelung and others.

Analysis of the New York Hospital Series—Since September 1932, 169 patients have been admitted to the New York Hospital and operated upon for varicose veins. Of this number, 121 cases have been followed for from one to six years after operation. Of the remaining 48, 20 are being followed but the operation was performed less than one year ago, while 22 have been lost to the Follow-Up Department. Reports on two patients were received through their family physician, and two reported by letter, these four are not included in the total analysis because they have not been examined in this clinic. Therefore, in this report 87 per cent of the patients operated upon have been followed, while 15 per cent have been lost to the Surgical Follow-Up Department.

There were two deaths from pulmonary emboli.

In the group of 121 patients, followed from one to six years, 178 extremities were operated upon, and our follow-up studies will be based upon this figure, for it represents a truer picture to refer to separate extremities than to individuals in whom a bilateral operation was performed.

Clinical Aspects—Although most writers, including Ochsner and Mahorney, find varicose veins more frequent in women than in men, the incidence in this series of cases is almost evenly divided between the two sexes as there were 63 males and 58 females. As a rule, there was no predilection for either the right or left extremity, a fact noted by Steubner, in his 104 cases in which both lower extremities were involved in 52 per cent, the right in 25 per cent and the left in 25 per cent of the cases. In our series, 96 (54 per cent) operations were performed on the left leg and 82 (46 per cent) on the right leg. There is an anatomic factor which might explain the slightly

greater incidence of varicosities in the left leg, namely, the iliac vein has to pass posteriorly to the right iliac artery and may, as a consequence, suffer more back pressure

The occupations in which the patients had been engaged varied, corresponding to general types of work performed by the clientele of the hospital as a whole. They included

Housewife	43	Business man	9
Domestic servant (male and female)	20	Factory worker	6
Counterman (butcher, baker, grocer)	11	Miscellaneous	20
Laborer			12
			<hr/> 121

The ages ranged from 22 to 77, and were distributed as follows

20-30	10	41-50	38	61-70	7
31-40	38	51-60	26	71 and over	2
					<hr/> 121

All patients were first seen in the Varicose Vein Clinic and then recommended for admission to the hospital because they were not suitable for injection treatment. If the varicose veins were associated with ulcer, the latter condition usually was healed first by bed rest, elastoplast bandage, Unna paste boot, or injection before admission. In a few instances, patients with ulcer were admitted and treated for it prior to operation. We feel that an ulcer can be healed and that every effort should be made to do so before operation.

In addition to the usual history and physical examination, and by far the most important preoperative step in this group, is a careful examination of the varicosities by someone familiar with the anatomy and pathologic physiology of varicose veins. The importance of determining a previous thrombophlebitis and early history of cardiac disease cannot be emphasized too strongly. It is only by the painstaking performance of all examinations that poor results may be eliminated.

The tests which are found most helpful in determining the extent of the disease are the Schwartz test, Trendelenburg test, Perthe's test and the comparative tourniquet of Ochsner and Mahoney.

The anatomy of the superficial veins of the lower leg has been carefully reviewed by Edwards⁸ and others. This venous system comprises the internal and lesser saphenous veins which communicate throughout with each other and, by communicating or perforating veins, with the deep circulation. The lesser saphenous vein empties into the popliteal vein in the popliteal fossa, while the internal saphenous, after receiving a group of superficial veins, meets the femoral vein at the fossa ovalis (Fig. 1). The importance of this group of veins is stressed repeatedly.

Operative Procedures—In the series of cases at the New York Hospital, six different operative procedures have been carried out.

(1) *Simple High Ligation*—Under local anesthesia, a 7 cm. incision is

made parallel to and 2 cm below Poupart's ligament. The midpoint of this incision is placed 2 cm medial to the femoral artery, which is identified by palpation. As the incision is deepened through subcutaneous tissues and fascia, a careful watch is kept for a bluish tint through the translucent fat, which indicates the proximity of the saphenous vein. This vein lies more medially, and is usually larger than one anticipates. In case the internal saphenous is not sighted, dissection of one of the tributaries will bring the operator upon the vessel. Dissection is facilitated by dividing the vein, one end of which is carried upwards—care being taken to keep within the fibrous sheath encircling the vein.

As the proximal end of the vein is exposed all branches are carefully divided and ligated, including the external pudendal, the external superficial femoral, the superficial circumflex iliac, the thoraco-epigastric and the superficial epigastric. These may enter singly into the internal saphenous, or in different combinations. They may even enter the femoral. The important point is that the femoral vein be visualized and exposed sufficiently to permit the accurate placement of a clamp and suture-ligature on the saphenous above the clamp. Another tie is now placed above the suture-ligature to prevent blood from coming in contact with the suture or injured intima. This tie is placed flush with the wall of the femoral vein but without encroachment upon its lumen (Fig 2). No stump should be left. A segment of vein, some 12 cm in length, is removed by continuing the dissection of the lower stump and ligating it. Closure of the wound is carried out in layers, black silk being employed throughout. An Ace bandage is applied and the patient gotten out of bed the day of operation. He is encouraged to walk about, but is not allowed to sit with the leg in a dependent position.

(2) *Simple High Ligation and Injection*—This is carried out as described above, save that after transfixing the distal stump, but before tying the knot, sclerosing fluid is injected into the lumen of the vein.

(3) *High Ligation with Excision*—A high ligation is performed, as described, and, in addition, other segments of the varicose veins are excised. In certain instances, this included the internal saphenous vein above the knee and, in a few cases, veins were excised both above and below the knee. These patients were kept in bed for a period varying from three days to two weeks before they were allowed to get up. Both deaths occurred in this group due to massive pulmonary emboli.

(4) *High Ligation and Low Ligation*—This procedure has been mentioned very seldom, but would appear to offer excellent possibilities, and avoids the difficulties and dangers of more extensive operations. It consists

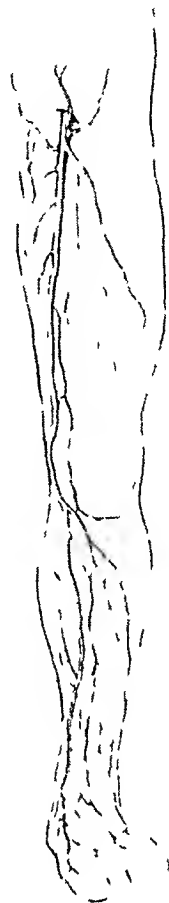


FIG 1—Showing the normal anatomy of the internal saphenous vein and its tributaries

of the simple high ligation with the addition of a simple ligation of the internal saphenous below an incompetent perforator, usually above the level of the knee. Recently, we have employed this procedure with the injection of a

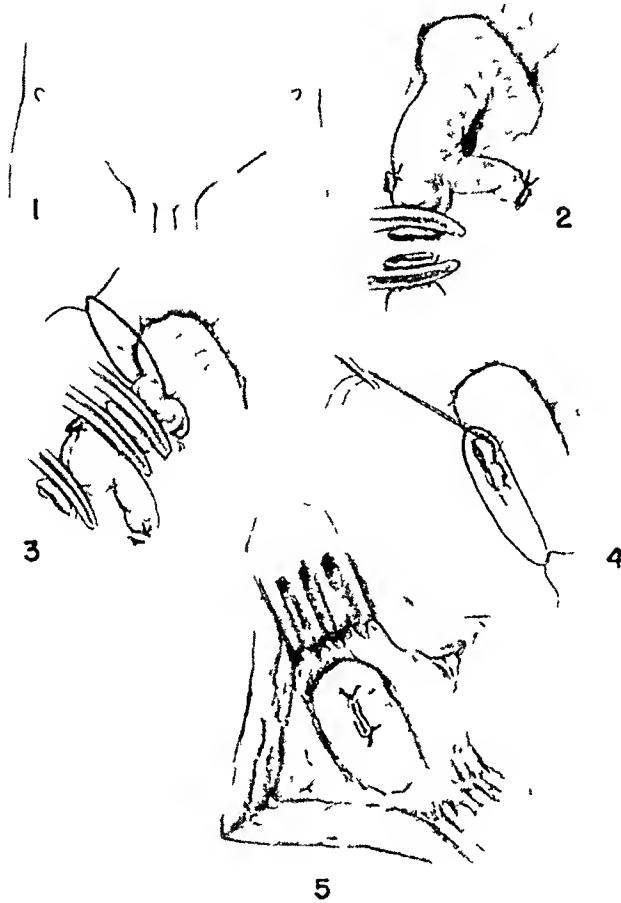


FIG. 2—SIMPLE HIGH LIGATION OF THE INTERNAL SAPHENOUS VEIN

- (1) The incision is placed parallel to, and below, Poupart's ligament, over the femoral vein
- (2) The vein is isolated and divided between clamps to facilitate dissection of the upper stump. All branches are carefully divided and ligated
- (3) When the saphenofemoral junction is exposed, a suture ligature is placed and the vein divided
- (4) A single tie is placed above the suture ligature to prevent the blood from coming in contact with injured intima
- (5) This shows the femoral vein with ligated stump flush with the wall but not encroaching upon the lumen of the vein

sclerosing solution at the time of operation, the cases, however, have not been followed a sufficient length of time for an accurate appraisal of its value.

(5) *Excision*—A simple excision of varicose veins was performed without a high ligation in a small number of patients. The procedure was carried out below the knee in most instances.

(6) *Low Ligation*—(Tiendelenburg operation) The simple ligation of veins in the mid thigh was occasionally used

Analysis of Results—In determining the results of the 178 operations upon 121 individuals, it was thought best to treat each extremity separately and to set up arbitrary standards. In almost every case the operation has been combined with injection, either before operation, to heal an ulcer, or after operation, to thrombose any varicose radicles.

The results are classified on the following basis:

(A) An excellent result—the patient is free of symptoms and without visible or palpable varicose veins. Ulcers are not present.

(B) A good result—the patient is free of symptoms, but with small varicosities which can readily be cared for by injection. Ulcers are not present.

(C) A fair result—there is improvement in the severity of the symptoms and evidence of varicose veins. Ulcers are not present.

(D) A poor result—there is no improvement in the severity of symptoms or in the size of the veins. An ulcer may or may not be present.

It will be noted in the above classification that a persistent or recurring ulcer immediately places the result in the category termed "poor." When there has been a question regarding results, the poorer classification has always been chosen.

RESULTS OF OPERATION

(1) *Simple High Ligation* 59 operations. In this group there were 21 results considered excellent, 23 were good, 13 fair and 2 poor. In one case, rated as a poor result, the patient did not return for injections, in the other, the operation was not sufficiently extensive.

(2) *Simple High Ligation and Injection at the Time of Operation* 14 operations. In this group of cases there were 9 results which were considered excellent and 5 good. There were no failures.

(3) *Simple High Ligation and Excision* 88 operations. In this group there were 47 results which were considered excellent, 30 good, 6 fair and 5 poor. The various causes of the poor results were apparently inadequate excision, poor selection of procedure, and disregard of evident contraindications to operation.

(4) *High and Low Ligation* 4 operations. The results were classified as excellent in 2, good in 1, and fair in 1. None of this group was considered a poor result.

(5) *Simple Excision of Varicose Veins* 8 operations. Although only a small number of cases were subjected to this form of treatment, it carried a high percentage of poor results. Two of the 8 cases were considered excellent, 1 good, 1 fair and 4 poor. In all of the 4 poor results, failure was due to inadequate surgery.

(6) *Low Ligation* 5 operations. The results prove the futility of this procedure. None was considered excellent, none good, 3 fair and 2 poor.

Again the patients with poor results were found to have had inadequate procedures

SUMMARY OF CASES

When the 178 operations for varicose veins are combined, it will be seen that the results, irrespective of method used, were excellent in 81, good in 60, fair in 24 and poor in 13 cases. This summary is shown in Chart 1.

TYPE OF OPERATION	TOTAL NUMBER	END-RESULTS							
		EXCELLENT		GOOD		FAIR		POOR	
		NO.	%	NO.	%	NO.	%	NO.	%
HIGH LIGATION	59	21	36	23	39	13	22	2	3
LIGATION AND INJECTION	14	9	74	5	39	0	0	0	0
LIGATION AND EXCISION	88	47	53	30	34	6	7	5	6
HIGH AND LOW LIGATION	4	2	50	1	25	1	25	0	0
EXCISION	8	2	25	1	12.5	1	12.5	4	50
LOW LIGATION	5	0	0	0	0	3	60	2	40
TOTAL	178	81	45	60	35	24	13	13	7

CHART 1—Showing the total cases for each type of operation, and the end results

TYPE OF OPERATION	DURATION OF FOLLOW-UP PERIOD								TOTAL
	1 YEAR	1 1/2 YEARS	2 YEARS	2 1/2 YEARS	3 YEARS	4 YEARS	5 YEARS	6 YEARS	
HIGH LIGATION	13	18	16	6	5	1	0	0	59
LIGATION AND INJECTION	2	4	4	0	2	2	0	0	14
LIGATION AND EXCISION	19	19	15	12	11	9	2	2	88
HIGH AND LOW LIGATION	1	0	2	0	0	0	0	1	4
EXCISION	2	2	1	1	0	2	0	0	8
LOW LIGATION	1	0	0	0	4	0	0	0	5
TOTAL	38	43	38	19	21	14	2	3	178
PERCENT	21	24	21	11	12	8	1	2	

CHART 2—The duration of follow up, cases grouped according to the length of follow up

Although the number of cases is too small to permit definite conclusions, each follow-up period is recorded according to the operative procedure and again subdivided according to the end-results. This is shown in Chart 3. There is little change in the comparative results from year to year.

An attempt was made to follow each patient from year to year in order to ascertain at which time a result might be considered permanent. In this study we were unsuccessful due to the irregularity of the time of follow-up visits and to change in examiners. It is our opinion, however, that poor results usually become evident one year from the time of operation.

In the total series of cases there were three instances of pulmonary emboli after operation, two of which terminated fatally. Both deaths occurred after a high ligation and excision. In reviewing these three histories, several factors of interest were noted. The patients were kept in bed some time after operation, the ligation of the saphenous vein was not flush with the femoral

If the cases treated by excision (8) and low ligation (5) are excluded from the total—and these procedures should be condemned save in very exceptional cases—there remain 165 operations with excellent or good results in 138, or 84 per cent. In only seven cases was the result poor, therefore, in only 4 per cent was there no improvement in symptoms.

The analysis of cases was carried further to show—in each case—the period of time elapsing since operation. The results of this study are shown in Chart 2, in which the cases are grouped according to the operative procedure and the length of follow-up. The average length of postoperative observation was 2 1 years, and all cases were followed for at least one year.

VARICOSE VEINS

vein in at least two cases, adequate exposure may have been sacrificed by omitting a third assistant at the operating table

SUMMARY —One hundred and sixty-nine patients, treated at the New York Hospital for varicose veins during seven years have been reviewed, with comments on certain clinical aspects. A description is given of the six types of operation employed in the treatment of varicose veins in this and other clinics, and the end-results compiled to show the comparative value of these various procedures. A comment is made on the cases which were considered failures

TYPE OF OPERATION	DURATION OF POST-OPERATIVE FOLLOW-UP AND RESULTS								
	1 YEAR	1 1/2 YEARS	2 YEARS	2 1/2 YEARS	3 YEARS	4 YEARS	5 YEARS	6 YEARS	TOTAL
	EXCELLENT	GOOD	FAIR	POOR	EXCELLENT	GOOD	FAIR	POOR	
HIGH LIGATION	13	18	16	6	5	1	0	0	59
	5 6 2 0	9 5 3 1	3 7 5 1	2 1 3 0	2 3 0 0	0 1 0 0			21 23 13 2
LIGATION AND INJECTION	2	4	4	0	2	2	0	0	14
	2 0 0 0	3 1 0 0	3 1 0 0		0 2 0 0	1 1 0 0			9 5 0 0
LIGATION AND EXCISION	19	19	15	12	10	9	2	2	88
	10 7 1 1	9 9 0 1	11 4 0 0	10 2 0 0	2 4 4 0	3 2 1 3	0 2 0 0	2 0 0 0	47 30 6 5
HIGH AND LOW LIGATION	1	0	2	0	0	0	0	1	4
	1 0 0 0		1 1 0 0					0 0 1 0	2 1 1 0
EXCISION	2	2	1	1	0	2	0	0	8
	0 1 0 1	0 0 1 1	1 0 0 0	1 0 0 0		0 0 0 2			2 1 1 4
LOW LIGATION	1	0	0	0	4	0	0	0	5
	0 0 0 1				0 0 3 1				0 0 3 2
TOTAL	38	43	38	19	21	14	2	3	178
	18 4 3 3	21 5 4 3	19 3 5 1	13 3 3 0	4 9 7 1	4 4 1 5	0 2 0 0	2 0 1 0	81 60 24 13

CHART 3 —Combines the data in Charts 1 and 2. The results are grouped according to operation, and length of follow up, to show the end results

CONCLUSIONS

(1) An accurate knowledge of the normal anatomy and of the pathologic physiology of the veins of the leg is necessary for the intelligent treatment of varicose veins. Enquiry into special factors in the history of the disease in the individual case, and physical tests of the circulation, cannot be omitted without giving rise to some poor results

(2) The operation is best carried out with the patient hospitalized, and with sufficient assistance at the operating table to guarantee good exposure and careful attention to detail

(3) Extensive operations are contraindicated because they carry greater risk of pulmonary embolism by necessitating longer rest in bed than do the simple procedures in which the patient can be gotten up immediately after operation

(4) The best results in this series of cases have been obtained with simple

high ligation of the internal saphenous vein, with injection of sclerosing fluid at the time of operation

(5) Any modification of operative procedure answers the requirement so long as the ligation of the saphenous vein is carried out at the saphenofemoral junction, and the tributaries in this region are divided. An operative procedure must be chosen which most nearly corrects the faulty vascular system in the individual case.

(6) If the perforators or valves of the saphenous vein are incompetent, operation followed by injections of sclerosing fluids offers the best chance of a permanent cure.

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THE PROBLEM OF CATGUT SENSITIVITY AND ITS RELATION TO WOUND HEALING¹

A PRELIMINARY REPORT

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EXPERIENCE with thoracoplasty wounds closed with catgut brings out the fact that healing is very frequently poor. Although such wounds are probably the most abused of surgical incisions, this factor alone does not seem to be an adequate explanation for the disappointing results obtained.

The suture material employed was singled out as one probable responsible factor because when silk was used throughout all stages, healing was very satisfactory. Thus, abuse of the wound by frequent reopening could be minimized in its importance and the suture material employed, emphasized.

The possibility of sensitization to the suture material was suggested because the instances of poor healing appeared to occur with surprising regularity during the earlier stages. The later stages all seemed to heal kindly.

Reviewing the literature failed to reveal convincing evidence that sensitization to catgut did or did not occur, and, therefore, elucidation of this point seemed highly desirable.

The Wound —The commonly employed posterolateral thoracoplasty wound is one of the largest wounds surgically produced, and the principal adverse factors which undoubtedly affect it can be summarized as follows:

(1) The parascapular mass of muscle is thick and narrow, reducing thereby its elasticity, and more directly transmitting tension as result of shoulder motion to the suture line.

(2) The jutting ledge formed by the uppermost unisected rib produces distortion in the wound of varying degrees.

(3) Excessive accumulations of fluid within the extrapleural subscapular space will tend to point at the weakest place in the extracostal wall, namely, the incision.

(4) The blood supply to the lateral flap of the incision is compromised by being transected at approximately right angles to its axis of supply. Some compensation is had from anastomotic sources, but the middle third of the wound is the farthest from such an additional source. The middle third of the wound can be considered on this basis the danger zone of the incision.

(5) Reopening of the wound in approximately three weeks, recurrently, is probably the greatest single direct insult.

The closure of such wounds in the cases to be considered is routinely with catgut, using size No. 00 for the deep muscle layer in a continuous stitch through-and-through the muscle mass, being interrupted, however, at several points. Size No. 000 catgut is very frequently used in a superficial layer,

¹ Presented in part before the Central Surgical Association, Ann Arbor, Mich, March 1, 1941.

including the superficial fascia and subcutaneous tissues. This is not always used but is employed in the majority of cases. It is uniformly a strictly interrupted layer. The skin is closed with interrupted black silk. Closures are occasionally affected by placing small interrupted catgut sutures in the fascial plane, using a multilayered, small bite, interrupted technic.

Occasionally, silk is used throughout, in which case the usual technic is observed, making a multilayered, small bite, interrupted closure. Comparison of these three types of closure offers a very interesting study. Uniformly, all of the wounds closed with silk, when reopened, present a remarkable restitution to normal of the fascial and muscular layers. The tissues are dry and the areolar planes are very easy to find, being well preserved. In contrast, the wounds closed by the more common method of bulk suturing of the muscle layers with catgut presents a widespread obliteration of all areolar planes within at least one inch of the original incision, and the tissues are replaced by edematous scar. Intermediate between these two extremes lies the wound closed by interrupted catgut. Here the fascial planes are fairly well preserved because of their more accurate approximation, but the edematous scar and obliteration of the areolar spaces is quite marked. These wounds are all, at the time of being reopened, approximately three weeks old.

The catgut used is put up in standard sizes. Its method of preparation is the usual one, except that it is iodized and tanned to insure sterility and to increase its persistence in the wound. The amounts actually left in the wound have been determined by carefully measuring all the loose pieces remaining after operation and subtracting this from the original lengths broken for the procedure. The figures thus obtained show that between 129 and 162 inches are actually left in the wound. An average figure would be 140 inches, or slightly more than the content of two tubes. This amount of catgut would weigh approximately 0.6 Gr.

Present Study—As suggested by the literature,^{3, 5} though after several unsuccessful attempts, an extract of plain catgut was made in Coca's solution by the following method. Two and one-half grams of plain (iodized but untanned) sterile catgut was thoroughly dried in an oven. This was then extracted in sterile Coca's solution for 48 hours, with agitation. The resultant mixture was passed through a Seitz filter. The solution was sealed in serum bottles and cultured to determine sterility.

Chemical analysis of this extract revealed 69.5 mg per cent total nitrogen, and 1003.3 mg per cent of iodine.

This extract seemed to give reliable results under adequately controlled conditions.

All patients admitted for thoracoplasty were subjected to the skin test and the results recorded. Following each stage, approximately two weeks post-operatively, the skin test was repeated. A total of 54 patients passing through the Service had a total of 113 skin tests. Distribution of the skin tests according to stages is given, and the results are presented in Chart 1 by Curves 1 and 2.

This extract is injected intradermally in 0.02 cc amounts, and each test is

controlled by a similar amount of plain Coca's solution injected intradermally in a nearby area. The reactions are read in 15-20 minutes and graded in the usual manner. The reactions are usually faded by 45 minutes, leaving, in cases of severe reaction, a small area of brown discoloration.

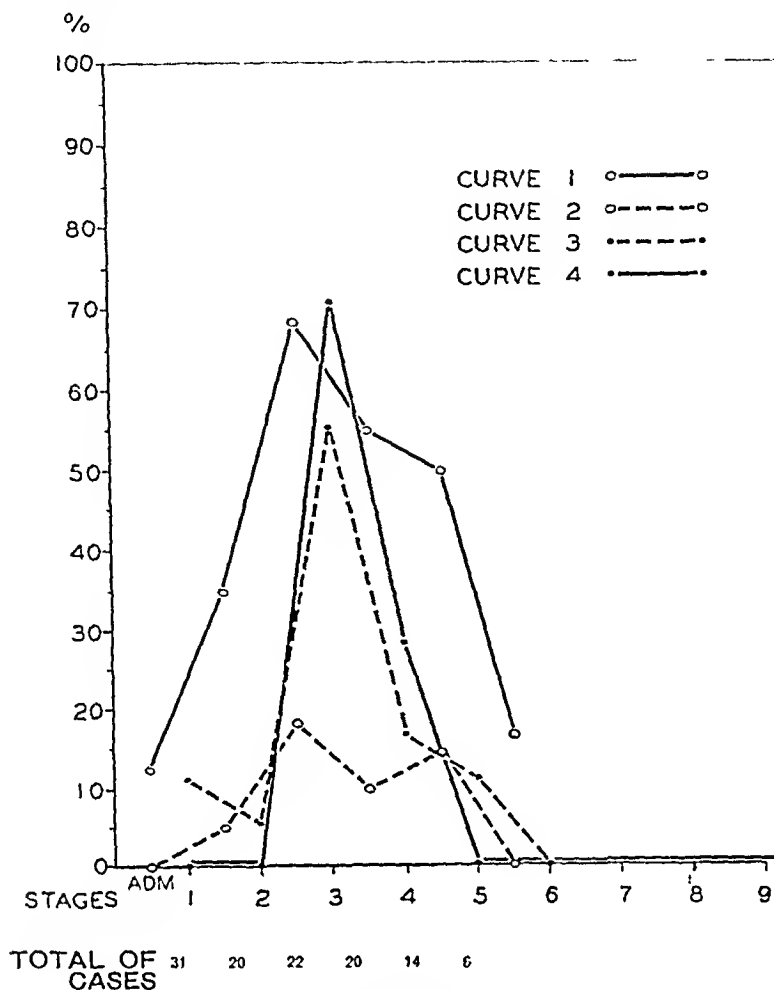


CHART 1
Curve 1—Represents percentage incidence of skin tests positive in any degree, by stages of thoracoplasty.
Curve 2—Represents percentage incidence of highly positive skin tests by stages.
Curve 3—Represents percentage incidence of all wound complications, by stages.
Curve 4—Represents percentage incidence of wound complications exclusive of infections, by stages.

Reference to the chart reveals the graphic representation of the skin tests. Curve 1 represents the percentage of reactions positive in any degree, among the patients tested at each period in the evolution of the thoracoplasty. Curve 2 represents the percentage of reactions that were highly positive at the same periods. Thus, on admission some 12 per cent of patients tested showed evidence of skin sensitivity but none of them reacted strongly.

The peak of sensitivity as estimated by the skin test, therefore, occurs after two stages of thoracoplasty or, in other words, after two exposures to catgut. Thereafter, the sensitivity fluctuates but returns to the original level after the fifth dose.

Curve 2, although necessarily low, is quite comparable to Curve 1.

The intensity of the response to the skin test was carefully compared to the severity of the inflammatory reaction in the next-stage wound and a surprisingly accurate prediction of the appearance of the wound could be made, it was

found, on the basis of the preoperative skin test. Thus, the severity of the apparent inflammatory reaction in the wound accurately paralleled the intensity of response to the skin test preoperatively.

A wound presenting a characteristically severe reaction is worthy of description. This could be seen as early as the beginning of the second postoperative day. Two features were present and will be described separately.

The first to become noticeable is redness along the wound margin. By the fourth and fifth postoperative days, this has extended to involve an area one to one and one-half inches around the wound. By this time the discoloration has assumed a brawny tint. By the sixth and seventh days the color is beginning to fade and desquamation may be seen. This takes place as small branny flakes. The reaction has largely subsided by the tenth postoperative day.

Shortly after the appearance of the redness, the presence of edema can be noted. This starts in the wound margins and extends, increasing in amount, until about the fifth or sixth day. At this time it may extend from the spine posteriorly well into the axilla anteriorly. The wound itself is moist, weeping, and its edges are rolled up, resulting in poor apposition. The edema subsides rather rapidly after the seventh day and has disappeared entirely by the tenth day.

After the reaction has subsided, the wound invariably presents considerable scabbing. The wound edges are irregularly apposed. The resulting scar is broad and irregular.

The foregoing description is, of course, the severest form observed. All grades of severity may be seen, and the mild reactions undoubtedly represent merely the exudative response to an absorbable suture material and must be considered as essentially normal.

Careful observation of these wounds revealed that the severest reaction any patient presented was regularly in the third-stage wound. This, of course, depends upon simple inspection and may be subject to error.

The wound complication that appears to be a direct sequela to this wound reaction resolves itself into a separation of the wound edges when some of the sutures, usually alternate ones, are removed. This separation most frequently occurs in the middle third of the wound where stress is probably greatest. The linear extent of this separation is determined by the distance left unprotected by the removed sutures. Such disruption permits escape of fluid from the subscapular extrapleural space, indicating separation of the muscle layers as well as the skin. This incident most often occurs at the fifth day, when one-half of the sutures are routinely removed.

One other observation on the behavior of such wounds has been that patients presenting mild skin sensitivity only, have been subject to exactly this complication. This fact appears at first to be somewhat contradictory. The answer is, however, readily forthcoming from the work of Kahn,⁴ who showed that various tissues of the body had different capabilities of reacting to antigens introduced into them. Thus, it has been observed that the extent of reaction exhibited by the muscle layers, as evidenced by widespread edematous, cicatricial obliteration of the areolar and fascial planes when a wound is opened

at a thoracoplasty-stage, is not always commensurate with the degree of skin sensitivity as measured by the skin test reaction. Thus, whereas the skin test mirrors very accurately the reaction to be seen in the skin and probably subcutaneous tissues at the succeeding stage, it does not necessarily reflect the extent of reaction in the muscle tissues.

Thus, at this point the practical value of the skin test decreases because while it will predict the appearance of the wound postoperatively, it may not tell the extent of underlying reaction. It is believed that this underlying reaction is, from a practical standpoint, far more important than mere skin sensitivity or reaction. This fact makes any estimate of the percentage accuracy of the skin test a matter of speculation.

The amount of reaction manifested by the skin can only be regarded as a measure of the ability of this layer to respond as a reacting system and not as a measure of the capability of the organism as a whole or any other specific tissue in particular.

The fact that the skin reacts as a unit system is demonstrated by the finding that reaction to the skin test is the same near the wound as it is at a distance from it.

This fact is further strengthened by the following observations:

(1) Using blood serum from patients presenting severe wound reactions, as well as four plus skin test reactions, passive transfer of antibodies was attempted in six different subjects. In no instance could such an occurrence be demonstrated.

(2) Using the extract as antigen, precipitins could not be demonstrated in the blood serum of these same patients.

(3) Using serum obtained from the extrapleural space of numerous patients, again, precipitins could not be demonstrated.

An explanation was sought for this apparent insecurity of catgut wounds in patients exhibiting marked sensitivity. Although the data herein presented is fragmentary because of fear that sinuses might be produced by any elaborate experimentation with these wounds, nevertheless an answer is suggested by the following experiment. A silk thread was securely tied around one of the subcutaneous catgut sutures in three first-stage wounds in nonsensitive patients. Lysis of the catgut, as indicated by freeing of the silk thread, occurred on the tenth day in one instance and on the twelfth day in the other two. In a patient exhibiting mild sensitivity at the end of the second stage, a similar experiment revealed the catgut thread in the third-stage wound to break at a slight tug on the sixth day. In a highly sensitive patient whose wound was opened by the sixth postoperative day, no evidence of remaining catgut was seen.

Thus, it would seem that in the presence of an hypersensitive response, lysis of the catgut sutures occurs with greater rapidity than in normal individuals.

Incidence of Wound Complications—The analysis of reactions seen in wounds is difficult because it is quite impossible to accurately weigh the proportionate responsibility of the many factors concerned in the healing of

wounds In order to eliminate, therefore, the factor of personal interpretation, the records of all thoracoplasties, unselectedly, were reviewed for approximately six months This included some patients prior to the institution of this study and does not include all patients who were skin tested It represents a comparable group, insofar as technique, surgeons, and care are concerned

No attempt was made to classify the various complications except to call wound infections those instances where the wounds were opened for drainage and pyogenic organisms were recovered by culture The infecting organism was a *Staphylococcus aureus* or the tubercle bacillus in every instance Two instances of tuberculous infection of these wounds are included

In this group there were included, of course, several patients who had had previous stages of thoracoplasty prior to this admission In such instances, the old records were reviewed and complications tabulated Thus, 45 patients underwent a total of 184 stages of thoracoplasty

Complications were recorded in 18 instances, or an incidence of 9.7 per cent Eliminating the frank wound infections, of which there were 11, or 5.9 per cent, leaves seven, or 3.8 per cent of complications of other types Four instances in this latter group of complications came under direct observation in this study and corresponded to the previously described reaction to catgut

This data can be graphically represented by Curves 3 and 4 of Chart 1 Curve 3 represents the percentage of all complications occurring at each stage Thus, it includes frank wound infections as well as those presenting only separation of the skin edges and leakage of extrapleural fluid Curve 4 represents the percentage of the complications exclusive of the infections occurring at each stage

When all complications are considered (Curve 3), the curve produced very closely parallels the curve of skin sensitivity (Curve 1) No complications were encountered after the fifth stage, and there was a total of 12 operations beyond this stage The high level at the first stage is in all probability accidental, being due to the rather unusual occurrence of infection in first-stage wounds within this group of patients

The striking feature in both of these curves is the fact that the peak of incidence for wound complications of any sort occurs in the third-stage wound, which represents the inoculation of catgut immediately following the peak of sensitivity as demonstrated by the skin test

SUMMARY AND CONCLUSIONS

Evidence has been presented that

(1) Sensitivity to catgut, used in rather large doses and repeatedly, can be demonstrated by means of a skin test

(2) The curve of the sensitivity closely corresponds to the immunologic response to the commonly used antigens

(3) It is intimated that in sensitized individuals, lysis of the suture material occurs more rapidly than in the nonsensitized person

(4) The reacting capacity of different fundamental tissues varies It is further suggested that although most often the skin is capable of greater

reaction than skeletal muscle and/or its fasciae, in some individuals even this relationship may be variable. It is believed that the reaction in the muscle layers is more important from a practical standpoint than that of the skin alone.

(5) The sensitization to catgut appears to be a purely local reaction, confined to the tissues as a reacting system since no evidence of systemic response has been seen.

(6) When the wound complications occur, they do so with amazing frequency at a period in the evolution of the thoracoplasty when sensitivity is highest, as demonstrated by skin tests.

It is believed that, insofar as wound complications are concerned, the only one that can be attributed to hypersensitivity to catgut is the result of a delay in the process of healing. Apparently, the first reaction to catgut is inflammatory, producing the redness and edema described. The result of this is early lysis of the suture material. The fibroblastic reaction is apparently delayed until this exudative reaction has subsided. Thus, it would be an intensification of the usual exudative reaction to catgut.

Some accessory factor, such as loss of support by removal of skin sutures or mechanical stress exerted by the scapula, is believed to precipitate such an occurrence. It can be averted by maintaining apposition of the skin edges for ten days, at which time healing should be fairly well advanced.

(7) The exact component of a catgut suture which acts as an antigen cannot be determined from this study alone.

According to the Wolff-Eisner hypothesis,⁶ the iodine present in the catgut could become antigenic by combining with serum in the wound. Jacobs² has shown that serum tends to lose its species specificity after iodination. It might further be in the iodine-catgut protein combination, or actually the catgut protein itself.

Rather conclusive evidence, however, has been brought out by Farris¹ that it is the protein itself. He obtained a very severe intra-ocular reaction around catgut in rabbits after sensitization of these animals to sheep serum. Such reaction did not occur in nonsensitized animals.

(8) The skin test has no practical significance in sorting suitable candidates for catgut closures because it is often only after one or two stages that sensitivity becomes demonstrable.

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THE RÔLE OF THE LIVER IN PREOPERATIVE CARE

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INTELLIGENT PREPARATION of the surgical patient requires an appreciation of varied physiologic principles. Although it may be desirable, it is difficult to formulate rules applying in all circumstances. Diseases and patients vary too much and fixed rules do not allow for the prompt application of new findings by chemists and physiologists. Preoperative care must, insofar as is possible, repair the damage to the whole organism which has been brought about as a result of disease. This concerns nutrition, water and salt balance, adequate oxygenation, and such matters. The patient must also be fortified to withstand the operative measures necessary for radical control of the disease. He must be able to destroy the anesthetic agent which is used, to compensate for the loss of blood and fluids which even the gentlest handling will bring about, and to withstand the effects of a period of shock. There must be a reserve sufficient to supply the needs of the body during the postoperative period when adjustments to metabolic disturbances must be made and when ordinary methods of providing nourishment have been suspended. In this era of generally good technical ability, the improvement in morbidity and mortality statistics depends more on the intelligent application of such measures than on improvements in technic. The limit of advance is our ability to maintain the patient's good condition during long procedures. Anesthesia has extended its possibilities, it remains for attention to details of preoperative care to extend the limits.

Knowledge of the physiology of the liver is essential for the understanding of many principles involved in preoperative care. It is the one organ in which many of the processes take place. Our information about its function is meager, but not so lacking as to justify an attitude of hopelessness. Too often, one hears there is no one satisfactory liver function test, with the implication that all tests may be disregarded.

There are many highly satisfactory methods of evaluating the ability of the liver to do its job. A consideration of its various known functions and methods of testing, restoring, or increasing those functions will be made. Particular stress will be laid on the more recent additions to our knowledge and to significant experimental work.

Blood Clotting—The liver is the site of the manufacture of the fibrinogen fraction of the plasma protein¹—normally, the serum contains about 250 mg per 100 cc. Fibrinogen is the soluble precursor of the insoluble fibrin in the clot. The serum content of this protein varies under different circumstances,

¹ Read before the New York Surgical Society, November 26, 1941.

apparently independently of the leukocyte count. It is elevated, among other factors, by abscess formation, moderate liver damage,² foreign protein injections, and fever, and decreased by severe liver damage and protein-deficient diet. The sedimentation rate of red cells is a rough index of the fibrinogen level, accelerating as the protein concentration increases.^{2a} Much work remains to be done on this protein. Its value as a test of the state of the liver or the ability to respond to blood-clotting demands has never been fully appreciated.

The liver is also the site of the manufacture of prothrombin. It is made from unknown substances, and is dependent on an adequate supply of vitamin K or some substance with vitamin K activity. With thromboplastin and calcium, prothrombin forms thrombin. Its level in the blood is easily determined by one of several methods. The absorption of vitamin K by the gastrointestinal tract is in combination with deoxycholic acid,³ obstruction to biliary flow, therefore, will prevent this absorption and the prothrombin deficiency is the cause of bleeding in jaundice.⁴ In severe damage to the liver that organ is unable to manufacture prothrombin, in spite of adequate supply of vitamin K or a substance with vitamin K activity.⁵

Heparin was first prepared from the liver by Howell but it has since been obtained from many other organs, notably the lung and intestinal mucosa. Its manufacture is in some way linked to the mast cells present in large numbers in the smaller blood vessels.⁶ It is stored to some extent in the liver.⁷ The prevention of thrombosis in the postoperative period is dependent on an adequate supply of heparin for the serum. The delicate balance between the coagulants and heparin, the body's anticoagulant, is important. The liver has a large measure of control over this balance. Disorders are rather an excess of clotting factors than a deficiency of heparin and the imbalance may be met by the administration of additional heparin.⁸ There is no known method for stimulating the production of heparin.

Detoxification—One of the earliest known functions of the liver is that by which it destroys noxious substances which enter the body. It has been known that any condition which interferes with the liver's ability to destroy poisons will produce rapidly disastrous effects. Studies of this function have generally been concerned with methods of rendering the liver susceptible to damage. Opie and Alford,⁹ in 1914, showed that a high fat diet would ultimately render the liver unable to withstand the administration of chloroform. This will be referred to later in a consideration of fatty liver. Ravdin and his coworkers¹⁰ have studied the influence of foodstuffs on the susceptibility of liver to injury and with many other workers have demonstrated that starvation and low glycogen content of the liver may bring about this susceptibility. Tests for the detoxification properties commonly used are the bromsulphalein and the tetraiodophenolphthalein blood clearances—simple measurements of the ability of the liver to withdraw these easily detectable dyes from the blood during a certain time-interval. Another test which has been designated by some as a test of the detoxifying property of the liver is the hippuric acid

synthesis test of Quick. This test is a measure of the ability of the liver to conjugate benzoic acid with glycine to produce hippuric acid which is excreted in the urine. It depends upon a satisfactory renal function. The test may measure another function of the liver, namely, its ability to manufacture the amino-acid, glycine, because the addition of glycine to the benzoic acid will produce a normal synthesis in the presence of parenchymatous disease of the liver.¹¹ The detoxifying property of the liver may be improved or restored by reestablishing a high glycogen content. A discussion of this topic involves the function of the storage of glycogen.

Storage of Glycogen—The storage of carbohydrates in the form of glycogen, the manufacture of dextrose from proteins and fats, and the maintenance of blood sugar level are functions of the liver. The level of glucose in blood represents a balance between the rate of supply from the liver stores and the rate of utilization by tissues other than the liver. The so-called normal sugar tolerance curve has no relation to the function of the pancreas. The liver is the only source of blood sugar in a fasting organism.¹² This function of the liver is tested by either levulose or galactose tolerance tests. In the presence of liver damage the slow return and elevation of the curve are characteristic. In ordinary circumstances the glycogen content of the liver can be elevated by high carbohydrate diet. In the absence of ability to take food by mouth this may be accomplished by glucose infusions into the blood stream. There are conditions when an infusion or carbohydrate ingestion will not build up the glycogen stores of the liver. They will be discussed later.

Storage of Protein—The normal seven grams per 100 cc. of plasma protein is divided into large heterogeneous groups by chemical salting into albumin and globulin fractions. The manufacture of fibrinogen which is part of the globulin has been discussed. Of the remaining plasma protein, probably all the albumin fraction, and some of the globulins are manufactured in the liver. The importance of adequate supplies of proteins need not be emphasized to a surgical group. The treatment and prevention of shock and proper wound healing are directly dependent on an adequate plasma protein level and a normal partition. In deficiencies of the liver affecting its ability to manufacture the albumin fraction, the ratio between albumin and globulin is disturbed. The albumin is known to maintain the greatest part of intraluminary osmotic pressure, the globulins exerting only one-fifth of the total attraction while taking almost one-third the total bulk. The edema from loss of albumin, then, is greater than would be expected from the proportion of total protein which is lost. It is this edema which interferes with wound healing in patients with gastro-intestinal diseases not supplied with proper protein intake before operation. The ability of the liver to supply serum albumin in sudden shifts of osmotic pressure is one great factor in combatting shock. The tests for protein deficiencies in the liver are serum albumin and globulin determinations. The total proteins in serum may be determined very easily by modern specific gravity methods. To restore sufficient proteins any one of a number of measures may be used. The most direct and quickest is the transfusion of

human plasma, and for osmotic pressure the most useful fraction is the albumin. This is necessary in the emergencies where a large amount of serum has been lost, such as in burns. In most circumstances a high protein diet will be sufficient to restore the protein. Elman¹³ has demonstrated that in patients who are unable to ingest a high protein diet, highly purified amino-acids may be used intravenously.

Bile Acid Conjugation and Circulation—Normally, the liver manufactures the bile acids by conjugating cholic acid and the amino-acids, glycine, and taurine. The source of the cholic acid is not entirely clear but the liver is almost certainly the site of manufacture. These bile acids form a very necessary function in the absorption of fats in the gastro-intestinal tract. The formation of cholic acid takes place in the intestinal mucosa but is dissociated before the fat is taken up by the lymph. The bile acids may thus serve to transport a considerable quantity of fat. On release the bile acid enters the blood stream directly, it does not traverse the thoracic duct with the fat. Through the portal vein to the liver, where it is secreted again, the circulation is maintained.¹⁴ This circulation cycle in man occurs about three times, the loss is through the feces. The sudden total drainage through biliary fistulae or the interference with circulation which biliary obstruction produces taxes the ability of the liver to conjugate more acids. The uniformly low rate of hippuric acid synthesis in this group of patients would indicate a shortage of glycine which is necessary for the conjugation of both hippuric acid and glycolic acid. The restoration of the hippuric acid by the administration of glycine or glycine-containing products is probably an indication that bile acid production has been resumed.¹¹ That some degree of circulation takes place in obstructive jaundice is shown by Shafiroff, Doubilet, and Ruggiero.¹⁵ In a dog with an obstructed common duct, bile pigment may be found in the thoracic duct within ten to 20 minutes after obstruction occurs.

Josephson¹⁴ has suggested a liver function test on the basis of the ability of the liver to clear the blood of injected cholate. Other tests of this function of the liver are analysis of the bile for free and conjugated acids, and blood levels of bile acids. Normally, most of the bile acids are conjugated with glycine or taurine. The occurrence of large quantities of unconjugated acids may be considered an evidence of liver damage. As in the conjugation of hippuric acid, glycine is an important material in the formation of normal bile acids. Restoration of normal function should be brought about by feeding of proteins with high glycine content. The bile acid formation and circulation seems to be entirely independent of other liver functions.

Storage of Fat—There has been a great deal of recent work reported by chemists and physiologists on the fat-storing property of the liver. Normally, 6 per cent by weight of the liver is stored fat. A propensity of the organ to store fat in concentrations higher than this is a definite pathologic condition. It has been known, since the work of Opie and Alford,⁹ in 1914, that such fatty infiltration renders the liver more susceptible to injury by chloro-

form and other toxic agents. Since 1922, and the use of insulin, the knowledge that in depancreatized dogs fatty liver follows, and this fatty liver may be prevented or cured by the feeding of raw pancreas,¹⁶ has stimulated many studies. We know now that fatty liver may be produced by starvation,¹⁰ high fat diet,⁹ common bile duct obstruction,¹⁷ vitamin B₁ and B₆ deficiencies,¹⁸ alcohol, chloroform, and many other factors. In the presence of large amounts of fat, the liver is rendered unable to store glycogen,¹⁰ to manufacture dextrose, to excrete dyes,¹⁹ and will, according to Connors,¹⁸ eventually produce cirrhosis of the liver.

Hershey and Soskin,²⁰ in 1932, showed that substances other than raw pancreas (the phospholipids, lecithin and cephalin) will prevent fatty infiltration. Since then many other materials have been demonstrated to have this lipotropic effect: choline, egg albumin, casein, gelatin and, finally, the sulphur-containing amino-acid, methionine. Dragstedt²¹ has reported the finding of a hormone in the external secretion of the pancreas, which he calls lipocain, that has a lipotropic action. Ralli and Rubin²² have reported that an extract removed from powdered meat, when added to a depancreatized dog's diet, produces fatty liver, whereas the powdered meat alone has no such effect.

Ravdin,¹⁰ in animal experiments, has shown that the liver may contain large quantities of fat and glycogen at the same time. The high glycogen content in such circumstances is no longer protective against injury by chloroform. The susceptibility is related only to the fat content. The protective action of glycogen in most instances is due to the fact that high glycogen indicates the absence of fat. In order to replace the fat, a lipotropic substance must be fed. Glucose alone is not sufficient. The most convenient and speedy method of supplying the lipotrope is by a high protein diet. Although Elman¹³ has demonstrated that nitrogen balance may be maintained by the intravenous administration of amino-acids, the preparation of such solutions is difficult and expensive.

Unfortunately, there is no test for the presence of fat in the liver. In large quantities it will interfere with the ability of the organ to perform many of its functions and will make it more susceptible to the effects of toxic substances. There is one clinical finding which is helpful. A liver which contains 10 per cent by weight of fat will generally be enlarged appreciably. The enlargement is the characteristic painless, smooth, round edge found in chronic alcoholics. It would seem that the measures which correct fatty liver might be applied to all patients without harm and particularly to those whose liver function will be taxed by a long and shocking operative procedure.

Pathologic changes in the liver, not related to a known function, have engaged the attention of many workers. The clinical similarity of the syndrome called "liver death" and thyroid crisis has been noted by clinicians. Boyce and McFetridge²³ remarked this similarity, and found with hippuric acid synthesis tests that thyroid disease disturbed the function of the liver in direct ratio with the disease clinical severity. Schmidt and his coworkers²⁴

feel that the liver damage is related to the duration and severity of the disease and that specific measures to correct the damage, glycine administration for instance, will lessen the risk. They also feel that the operation of thyroidectomy has a damaging influence on liver function. Bartels,²⁵ expressing the feeling of the Lahey Clinic group, feels that the liver changes are directly due to the thyroid disease and are the pathologic factors in thyroid crisis. Experimentally, there seems to be evidence that another factor must be added to the hyperthyroidism to produce the characteristic central liver necrosis. Sealy²⁶ has induced the liver changes in rabbits when an infected warty growth of the skin was present at the time of the production of hyperthyroidism. He infers that the clinical occurrence of liver necrosis may be dependent on some added factor such as infection or anesthesia.

Other effects of feeding of specific proteins on liver should be noted. Mori²⁷ found that adding protein in the form of kidney feedings to a rice diet will protect rats from the carcinogenic effect of butter yellow on the liver. Rhoads and a group²⁸ at the Memorial Hospital have shown that casein and riboflavin supplements to a basal diet have a striking protective effect against the same carcinogen in rats.

There are tests of liver damage which have no relation to function and which parallel no function test. One of these has become especially valuable and should be mentioned. Hanger²⁹ described the peculiar property of serum from a patient with parenchymatous liver disease to flocculate a suspension of cephalin in cholesterol. This test is not only valuable for diagnosing liver damage but is also helpful in differentiating obstructive from hepatogenous jaundice.

To summarize, certain aspects of the physiology of the liver as it is related to the problems of preoperative surgical care have been reviewed. Some of the more recent contributions of the chemistry laboratories have been considered in the light of clinical needs.

There is definite evidence that the liver can be fortified against injury or impairment of its functions by specific measures. The feeding of glycine in pure form or in a protein diet will bring about a normal ability on the part of the liver to conjugate hippuric acid from sodium benzoate and probably to conjugate glycocholic acid from cholic acid. The feeding of a high protein diet and perhaps some substances, lipocalc or choline, will promote the removal of fat from a fatty liver or prevent the deposition of fat under conditions which ordinarily produce the changes. There is convincing evidence that fatty liver is not only more susceptible to damage but may be a factor in the etiology of such conditions as thyroid crisis.

The liver's control over blood sugar levels, over plasma proteins, over bile acid manufacture and secretion, and its part in the complex mechanism of blood clotting and detoxification, have been considered. Many of the latest additions to our knowledge are in the animal stage. It remains for clinical surgeons to confirm or deny the application of these findings in the human.

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BRIEF COMMUNICATION

THE ADVANTAGES OF COMBINING LOCAL INFILTRATION ANESTHESIA WITH CONTROLLED FRACTIONAL SPINAL ANESTHESIA IN SUBSTANDARD SURGICAL RISKS

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OCCASIONALLY, in the practice of most surgeons, celiotomy must be performed upon patients who are bad risks for any type of anesthesia. When the character of and the site where the proposed procedure is to be carried out is accurately known, it is usually possible to employ local anesthesia, which most physicians agree entails the least risk for the patient.

Unfortunately, it is sometimes impossible to arrive at an exact diagnosis preoperatively and there are other cases in which one can feel reasonably certain of the diagnosis but in which the possibility of error persists. In such situations, and in bad risk patients, one is confronted with the following dilemma. On the one hand spinal anesthesia may be employed which will provide adequate exposure for whatever is encountered but entail considerable risk for patients with impaired circulation. On the other hand, local anesthesia may be used which will too frequently have to be supplemented with an inhalation anesthetic if the exposure and relaxation are not adequate. This often means a deep ether anesthesia with a difficult induction after the peritoneum is opened.

The use of Lemmon's apparatus for controlled fractional spinal anesthesia makes it possible to avoid this dilemma. The spinal puncture is done, the point of the needle left in place within the subarachnoid space, and the other end connected by rubber tubing to a syringe containing 500 mg of procaine hydrochloride dissolved in 10 cc of spinal fluid. However, none of this solution is administered at once. Instead the operation is begun under local anesthesia, exposing the patient to the minimum risk in opening the abdomen. After the abdomen is open, if the procedure indicated can be satisfactorily completed under local anesthesia, no spinal anesthesia is given. If, on the other hand, the necessary procedure requires extensive exploration or more relaxation, spinal anesthesia may be given in its safest form and maintained during such part of the procedure as is necessary. If it does cause a substantial drop in blood pressure and, this cannot always be avoided when the patients are on the verge of shock, the withdrawal of spinal fluid will usually shorten its action.

We have used continuous spinal anesthesia for nearly all abdominal cases, except appendicectomies, during the past 15 months. There have been no

table deaths, relaxation has been as perfect as with nupercaine, the anesthesia has been continued as long as four and a half hours, patients have been encountered who required several hundred milligrams of procaine hydrochloride, while others have been anesthetized to the costal margins with as little as 75 mg

Thus, we have confirmed all the major claims of Lemmon for his method

Although we have not employed the deferred method in a large group of cases, it has seemed to offer sufficient advantages in a limited field to warrant recommendation. Illustrative case records are summarized below

The first two cases are those of patients, nearly moribund it is true, whom we dealt with before the use of controlled fractional spinal anesthesia. In one we chose the first horn of the dilemma and with the other we chose the other horn. Both patients died on the table

The next is a patient in whom it was possible to omit the spinal anesthesia entirely, that is, the procedure was completed with local

The last two required spinal anesthesia and small amounts were successfully administered during the critical stages of the procedure only

Case 1—A R, Hospital of the University of Pennsylvania, #43581. Age 65, white, male, admitted 12-19-39

The patient had meningovascular lues and tabes dorsalis. He also had cerebral arteriosclerosis with facial palsy and had recently had an anterior coronary occlusion

At 4 00 P M he developed abdominal pain and on admission had a tender, resistant distended and silent abdomen. The preoperative diagnosis was peritonitis due to a ruptured viscus. Appendicitis with rupture at the base was considered most probable

Operation—A low spinal anesthesia was given by the single injection method but it was not very effective so the operation was begun with local anesthesia. The appendix was exposed through a McBurney incision. The peritoneal cavity contained large amounts of pus but the appendix was not ruptured. In order to explore the remainder of the abdomen general anesthesia was necessary. Cyclopropane and ether were used and a rupture was found in the sigmoid but the patient died on the table

Case 2—E C. Graduate Hospital of the University of Pennsylvania, #146662. Age 45, colored, male, admitted 7-26-40

The patient had had a ruptured duodenal ulcer 5-25-40 followed by evidence of a pelvic abscess which subsided without drainage. He was readmitted following vigorous catharsis with cramp-like pain, vomiting and a temperature of 102° F. Pulse rate was 130 and blood pressure 100/80. The abdomen was tense and distended. He was managed with suction drainage and supportive treatment for several days but finally the obstructive symptoms became definite and operation became necessary

Operation—Spinal anesthesia with nupercaine was employed. The relaxation was excellent. A distended loop of bowel was found and an enterostomy performed but the patient died on the table as the wound was being closed

Case 3—J O'D. Graduate Hospital of the University of Pennsylvania, #149426. Age 36, white, male, admitted 1-30-41

The patient was greatly overweight. He had been having precordial pain on exertion for five years and an electrocardiogram showed evidence of coronary disease. He had had indigestion for ten days and had moderately severe epigastric pain from 1 00 P M on 1-30-41. Maximum pain and tenderness were to the left. As they did not subside operation was decided upon the next day

Operation—A malleable needle was inserted in the back and connected by a tube

to a syringe containing 500 mgs of procaine in 10 cc of spinal fluid. Operation, however, was begun under local anesthesia. Acute cholecystitis and the edematous form of pancreatitis were found and cholecystostomy performed. No spinal anesthesia was necessary and none was given. The patient made a good recovery.

Case 4—M. D. Pennsylvania Hospital, #58321. Age 65, white, female, admitted 4-6-41.

The patient had been treated for carcinoma of the cervix with radium in May, 1940. She had had diarrhea intermittently after that treatment and had been under the care of a cardiologist for attacks of auricular fibrillation. At the time of admission she had abdominal pain and vomiting, the abdomen was distended and tender. The patient was irrational and there were moist râles at both bases and some evidence of bronchopneumonia. The preoperative diagnosis was peritonitis and intestinal obstruction.

Operation—Celiotomy was performed under local anesthesia and exploration and cecostomy under spinal anesthesia administered by our modification of the method described by Lemmon. Procaine was given at intervals of from five to 16 minutes. The successive doses were 25 mg, 25 mg, 12 mg, 12 mg, 12 mg, and 12 mg. The systolic blood pressure varied only between 120 and 108 Mm. of mercury. During the procedure 250 cc of plasma was infused. The patient left the operating room in comparatively good condition.

Case 5—A. M. Bryn Mawr Hospital #1042170. Age 67, white, female, admitted 3-1-41.

The patient was admitted with signs of intestinal obstruction. She improved greatly after intubation with the Miller-Abbott tube and the obstruction was localized to the lower ileum. In spite of the improvement she continued to have a marked azotemia and râles at both lung bases. There was no history of coronary infarction but her physician did not believe that she had much cardiac reserve. She was quite obese.

Operation—She was operated upon under local and controlled fractional spinal anesthesia. The abdomen was opened before any procaine was administered intrathecally. It was then found that the site of obstruction was deeply placed. Small doses of procaine were given and only then was it possible to expose and free an adhesion in the pelvis. The total amount of procaine given intrathecally was 75 mg and this amount did not cause a serious drop in blood pressure.

CONCLUSIONS

Exploratory celiotomy is occasionally necessary in patients who are very poor operative risks.

The use of Lemmon's procedure for controlled fractional spinal anesthesia makes it possible to operate on these patients under local anesthesia and yet to switch to controlled spinal anesthesia if a condition is found which requires a greater exposure or more relaxation than the local affords.

We believe that this combination of anesthetic techniques further reduces the combined dangers of anesthesia and intra-abdominal manipulation for this type of case.

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CORRESPONDENCE

TO THE EDITOR

In an article entitled "Tumors of the Carotid Body," by S W Harrington, O T Claggett, and M B Dockerty, published in the November, 1941, issue of the ANNALS OF SURGERY, it is stated (1) That the carotid bodies are homologous to the medullary portion of the adrenal medulla, and (2) that their function is negligible because bilateral extirpation may be performed without untoward symptoms

Actually, the carotid bodies, together with the aortic body (a similar structure situated between the arch of the aorta and the pulmonary artery) are now known to have an unique and irreplaceable function because they contain sensory end organs that respond to certain chemical changes in the arterial blood. These sensory receptors (now called chemoreceptors or chemoceptors) can be stimulated by a decrease in oxygen tension, or by an increase in CO_2 tension or acidity in the arterial blood, and by certain drugs and chemicals such as nicotine, lobeline, cyanide, sulfide, etc. The result of stimulation of these chemoreceptors is a marked increase in respiration and blood pressure, the afferent pathways are the two carotid sinus and two depressor nerves, entering the central nervous system by way of the glossopharyngeal and vagus nerves respectively.

The carotid bodies should be of particular interest to the surgeon for several reasons. First of all, it is now known that reflexes from these structures constitute the main defense of the body against anoxemia, the stimulation of the respiratory and vasomotor centers that occurs in periods of oxygen deficiency is certainly due preponderantly, and perhaps entirely, to carotid and aortic body reflexes. Lack of oxygen probably does not stimulate the medullary centers directly at all, as formerly believed, in fact, if the carotid and aortic bodies are denervated anoxemia becomes purely depressant to the vital centers and respiration and blood pressure, instead of increasing, rapidly fail. Fortunately, this chemoreceptor reflex system possesses a ruggedness which enables it to maintain respiration and circulation reflexly even though the medullary centers are severely depressed by such agencies as prolonged anoxemia and deep anesthesia.

It is true that bilateral extirpation of the carotid bodies may not lead to untoward symptoms but this is due to the fact that the aortic body is never removed surgically and this structure can assume some or all of the functions of the carotid bodies. Even if the carotid and aortic bodies were removed, there probably would still be no outward signs of their absence until the organism was exposed to oxygen lack, in which case the vital functions would undergo steady and progressive deterioration without any stimulant phenomena whatever.

The original studies of carotid body function were made by C Heymans, in Ghent, in 1931-1933 in recognition of which he was awarded the Nobel Prize in Physiology and Medicine in 1938. A number of review articles dealing with the functions of the carotid and aortic bodies have been published recently (*Ergebnisse der Physiologie*, 41, 28, 1939, *Annual Review of Physiology* 1, 185, 1939 *Physiological Reviews*, 20, 115, 1940, *Jour Lab and Clin Med* 26, 223 1940).

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LATERAL ABERRANT THYROIDS*

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IN PRESENTING another small group of cases of a relatively rare lesion, we have no desire to burden the literature with needless repetition. There has been, however, in recent publications, some difference of experience. Crile, 1939, made the following statements: "(1) Twenty cases of papillary carcinomas of the thyroid, 15 cases of papillary adenomas of the thyroid, and 13 cases of papillary tumors arising in lateral aberrant thyroid tissue are reported.

"(2) In only five of the 20 cases of papillary carcinoma of the thyroid has death occurred as a result of the tumor.

"(3) In no instance has it been proved that either regional or distant metastasis took place.

"(7) Tumors arising in lateral aberrant thyroid tissue are essentially benign. Only two of the 45 patients classified in the literature as having malignant tumors of lateral aberrant thyroid origin have been reported to have died as a result of recurrence of the tumor following operation. None of the 13 patients in this series has died as a result of lateral aberrant thyroid disease.

"It (8) has not been proved that either distant or local metastasis occurs from papillary tumors of lateral aberrant thyroid origin."

Lahey, Hare and Warren (1940) state that "We have had 36 cases of malignancy of the lateral aberrant thyroid bodies in which operation was performed, and two patients have died of recurrence." Cohn and Stewart (1940) who report 16 cases of malignancy, state that "Local or regional recurrence after incomplete operation occurred in 71 per cent of the cases of papillary tumor, but none of the patients with pure papillary tumors died of remote metastasis."

Ward (1940) on the other hand, reporting 12 cases of malignancy states that "In this series, two deaths from papillary tumors occurred, one of

* Submitted for publication May 1, 1941

these from pulmonary metastases, and I believe that a third death was caused by metastases from a lateral nonpapillary tumor. In view of these findings, I feel that a guarded prognosis should be given in similar cases, and that more deaths will be found in cases reported by other investigators if a sufficiently long period of observation is maintained."

Our own experience leads us to agree with Waid, and we wish to present it so that we may urge a serious surgical approach to what may appear at first study as a relatively benign lesion. At least some of the late, unexpected deaths we hope may be avoided if the problem is approached from this point of view. *Tumors in 27 of our 30 cases of lateral aberrant thyroid, malignant tumor in 23 of these 27, and eight deaths in these 23, or a 34 per cent mortality*, furnish the basis for our argument.

The term "aberrant thyroid" was first suggested by Schiager in 1906, and defined by him as "a mass of tissue having the structure of a normal or pathological thyroid gland and situated at some definite distance from the normal thyroid with which it has no connection whatsoever." Schiager gives credit to von Haller for first recognizing the condition in 1779, and the first adequate description was presented by Porta in 1849.

Distinction must be made between medial and lateral, as well as between true and false aberrant thyroid glands. It is accepted that medial aberrant thyroids are found along the thyroglossal tract, and these are not considered in this report. A false aberrant thyroid retains connection with the main gland—as a protrusion from it. This paper will be concerned only with true lateral aberrant thyroids.

Following Schiager's description, excellent summaries have been made by Billings and Paul (1925), Leech, Smith and Clute (1928), Dunhill (1931), Cattell (1931), Moritz and Bayless (1932), van den Wildenberg (1934), Crile (1939), Cohn and Stewart (1940), and Ward (1940). We have reviewed the literature to date and have been able to find 215 cases reported in detail. To this number must be added 36 reported by Lahey, Hare and Warren (1940), but these have not been analyzed. Of the 215 cases analyzed, 86 were considered definitely malignant. Of these, 66 were papillary tumors.

One of us (Rogers) has long been interested in the embryologic development of the thyroid, and it is worth a brief review, as it bears upon the surgical, anatomic and pathologic findings.

The description by His (1885) of the development of the human thyroid was accepted by anatomists as correct until it was contradicted by Grosse in 1910. His stated that the thyroid arose from three embryonic parts—one median anlage which developed from the floor of the pharynx and two lateral anlagen which arose from the last pharyngeal pouch. These three embryonic parts fused and developed into the thyroid gland.

Grosse thought the lateral thyroids, or ultimobranchial bodies, degenerated subsequent to their fusion with the median anlage. He consequently criticized the term lateral thyroid as being inaccurate.

In 1914, and again in 1939, Kingsbury agreed with Giossei, but stated that the human material available was not perfect for such a cytologic study. As a result his conclusions were made with reservations. In 1923, Kingsbury suggested a reinvestigation of the histogenesis of the thyroid on some mammal whose embryos could be attained in fresh condition. It was also necessary to have a large number of embryos of known ages to form a series of successively older stages.

In 1927, Rogers made a study of the histogenesis of the thyroid in the rat. This work was done in a closely graded series of approximately 300 embryos, fetuses and newborn animals. In this material mitoses and not degenerating cells were observed in the cell cords and masses derived from the ultimobranchial body. Since colloid-containing follicles developed in all of the cords in the region where the lateral thyroid was located, he concluded that the lateral thyroid (ultimobranchial body) formed some thyroid parenchyma which could not be distinguished histologically from any other part of the gland. In all probability the actual mass of thyroid tissue is relatively small.

Badeitscher (1918), studying pig embryos and fetuses, had arrived at a similar conclusion. In 1933, Weller, studying human embryos, verified the above observations. However, we consider Weller's estimate, that the lateral thyroid contributes one-third of the tissue of the definitive thyroid, much too high. Norris (1937) considers that the lateral thyroid contributes about one-sixth to one-eighth of the thyroid parenchyma.

Rogers suggested that the strongly determined median thyroid cords might induce the less strongly determined lateral thyroid anlagen to develop into a greater amount of thyroid tissue than is the case when the two structures remain separate. Godwin (1937, 1939) endorsed this view as being highly probable.

True lateral aberrant thyroid masses do not necessarily represent the same embryologic material. For instance:

(a) In lingual thyroids any lateral aberrant thyroid tissue would be derived entirely from the lateral thyroid (ultimobranchial) bodies and would probably, though not necessarily, be associated with the parathyroid derived from the fourth pharyngeal pouch.

(b) In most instances lateral aberrant thyroids are derived from the lateral thyroid body, and cell cords from the lateral cornu of the median anlage which have fused together but have become separated from the main part of the median anlage.

A mechanical explanation for the failure of the lateral thyroid (Fig. 1) to descend is logical. The epithelial ductus pharyngobranchialis connecting the lateral thyroid with the pharynx may not rupture. Likewise the ectodermal cleft IV (ductus branchialis), which is fused to the fourth pouch, may also persist. Both of these structures are shown in Figure 1A in a human embryo of approximately six weeks (10 mm in length).

The persistence of the ectodermal ductus branchialis after the rupture

of the entodermal ductus pharyngobranchialis probably explains the superficial position of our Case 3, where the tumor lay superficial to the first layer of deep fascia covering the sternocleidomastoid, but covered by the platysma, and possibly Case 12, although only the superficial part of this infiltrating growth was exposed. The platysma is derived from mesoderm of the hyoid arch, which grows downward and covers over the small third and fourth arches and their branchial ducts.

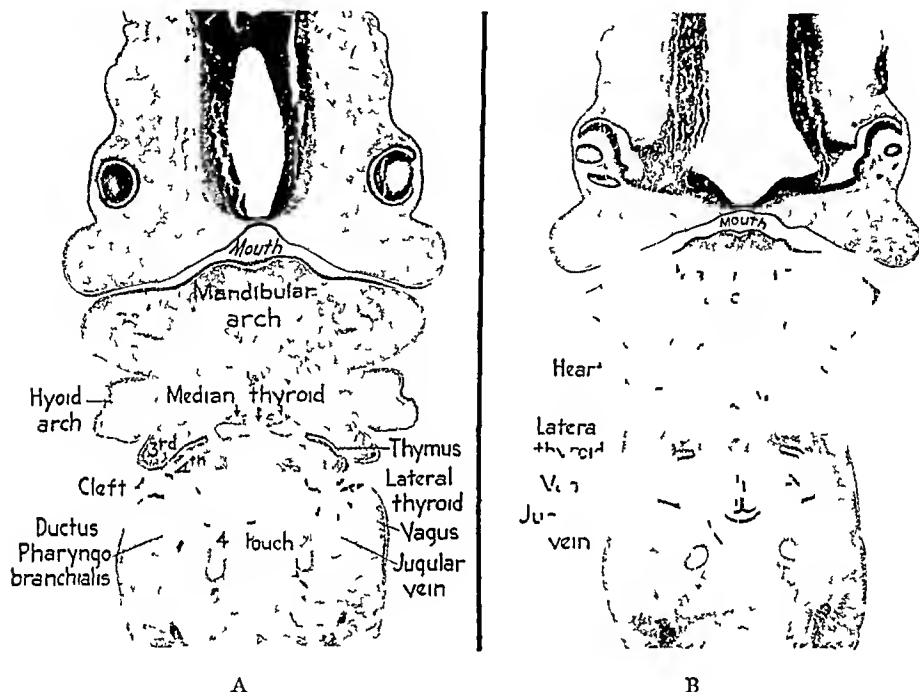


FIG 1—(A) A frontal section through the branchial region of a human embryo about six weeks of age (length 10.1 mm), showing the four branchial arches and the ectodermal clefts which separate the arches from each other externally. The fourth pharyngeal pouch is in contact with the ectoderm of the fourth cleft. The entoderm of the dorsal part of this pouch will form the superior parathyroid. Extending caudally from the medial part of the fourth pouch is the lateral thyroid body. A part of the median thyroid is shown adjacent to the third aortic arch. (B) A section through the same embryo (17 sections ventral to Figure 1 A). It shows the lateral thyroid cut transversely.

Rarely is a lateral aberrant thyroid found above the level of the twelfth nerve in the submaxillary triangle. This is true because the median anlage does not expand laterally far enough to make contact with the lateral thyroid until it reaches this level in its descent. Since the lateral thyroid arises from the pharynx below the level of the twelfth nerve, tissue derived from this source must, of necessity, be located below this level.

It is easy to understand how loose cords or masses of thyroid tissue may be stranded along its descent from about the level of the junction of the common facial (or comparable vein) with the internal jugular vein down to the lower border of the thyroid gland, and intimately associated with the lymphoid tissue in this location. Most of these aberrant masses are related to the internal jugular vein or its tributaries which are close to the thyroid during its descent.

The relations of the medial and lateral thyroid components, the parathyroids and the thymus, to each other and to adjacent cervical structures in embryos of about seven weeks are shown in Figures 2 and 3. Lateral aberrant thyroids, occurring below the level of the thyroid, probably develop from thyroid cords which have come in contact with the thymus. Such masses may be deposited along the course taken by the descending thymus even as far caudal as the superior mediastinum. In Case 26, where a total thyroidectomy and bilateral neck dissection were performed, the patient, after some months, no longer required thyroid extract. It is possible in this case, therefore, that there is still functional thyroid tissue, and presumably this is in the superior mediastinum, the only region which has not been explored. The relations of the embryonic thymus are illustrated in Figure 2.

No experimental evidence has been introduced since this type of experimental embryology can not be undertaken on mammals. However, some natural experiments aid in understanding the rôle played by each component, but are not conclusive.

Cases have been reported in which myxedema followed removal of a lingual (medial) thyroid which had not fused with the lateral anlage—indicating that the maximum potentialities of the lateral anlagen do not materialize when fusion with the median thyroid fails to occur.

Erdheim (1904) reported that in thyroaplasia the defect was of the middle anlage and that the lateral thyroid gave rise to no thyroid tissue. In Weller's myxedematous case (Ophelia P.), colloid-containing follicles definitely derived from the lateral thyroid are evidence that this embryonic part can and does produce thyroid-like follicles. Nor is there reason to doubt that the lateral as well as the median anlagen may be involved.

It is a curious fact, however, that there is no proof in man of function in lateral aberrant thyroids, and our Case 2, in which a toxic nodular thyroid

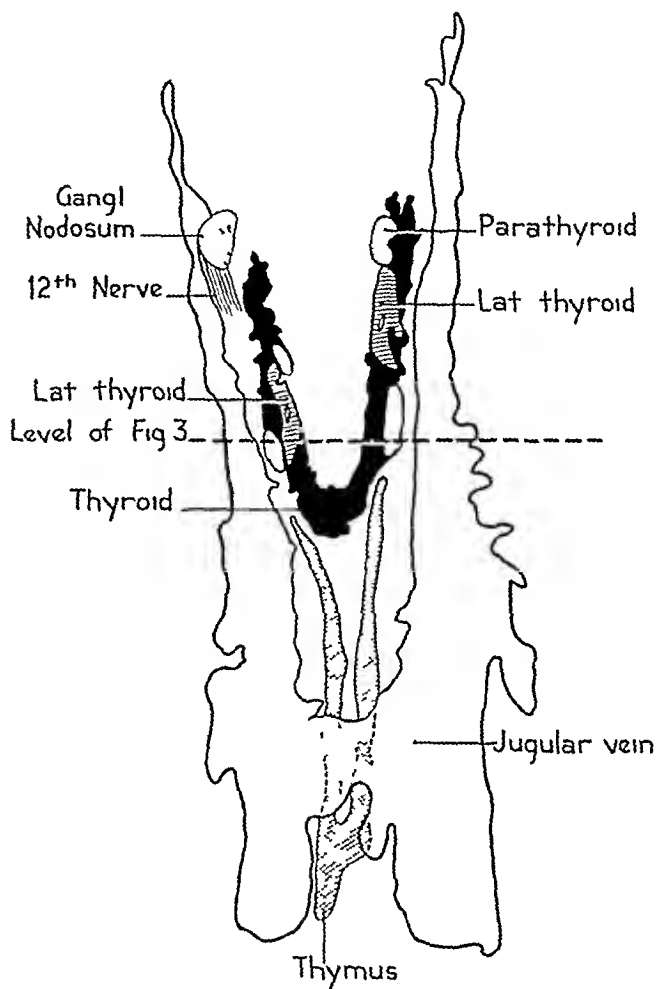


FIG 2—A reconstruction of the cervical region of a human embryo about seven weeks (length 22 mm), illustrating the relative positions and sizes of the median and lateral thyroid bodies, the two pairs of parathyroids, the right and left thymus, the internal jugular veins, the 12th cranial nerve, and the ganglion nodosum of the vagus. The horizontal line represents the level of the section illustrated in Figure 3.

was removed, and the lateral aberrant tissue showed no evidences of hyperactivity, is of interest in this connection. Also, we have been unable to find in the literature a case in which removal of a lateral aberrant thyroid predisposed the patient to hypothyroidism. Probst and Agnass (1936) reported a case of myxedema following removal of an aberrant thyroid tumor. They were indefinite as to the exact location of the tumor, and from their de-

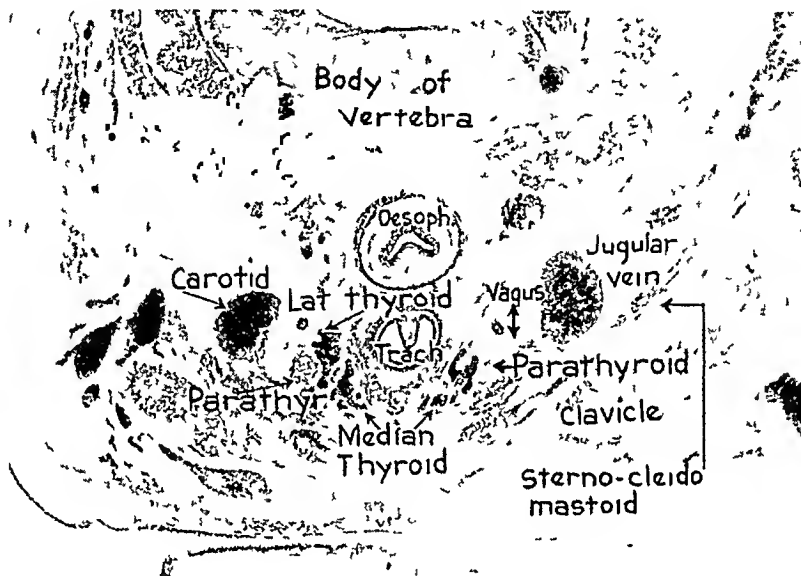


FIG 3—A transverse section through the cervical region of the embryo illustrated in Figure 2. On the right side the large lateral thyroid mass is intimately fused to the cords of the medial thyroid. The inferior parathyroids are present on both sides.

scription we believe that it should be regarded as a median aberrant thyroid. We encountered no cases of hyperthyroidism that were benefited by removal of lateral aberrant thyroid tissue alone. But it must be remembered that functional thyroid tissue is always present in the main gland.

Anatomically, as found at operation in our series, and as would be expected from a knowledge of the embryologic development, nearly all of the nodules lie beneath the sternocleidomastoid muscle. They may project from beneath the borders, and some are entirely behind the muscle in the posterior triangle, including the supraclavicular space. But they tend to occupy the same general location as the chain of deep cervical lymph nodes, from the posterior belly of the digastric muscle to the clavicle, none above the hypoglossal nerve. Except in advanced malignancy the lower nodules have been found lying loosely in areolar tissue from which they are easily shelled out, whereas the upper and midcervical nodules have more frequently been adherent to vein and muscle. The lowest nodule found lay below the lower pole of the thyroid gland. When the thyroid gland is involved with associated nodules these are found predominantly in the upper part of one lobe always on the affected side.

LATERAL ABERRANT THYROIDS

The diagram (Fig 4) depicts a composite view of the location of all of the nodules, or groups of nodules in all of our cases, as if all were in the left side of the neck. Thus, it is found that the three dominant sites are (1)

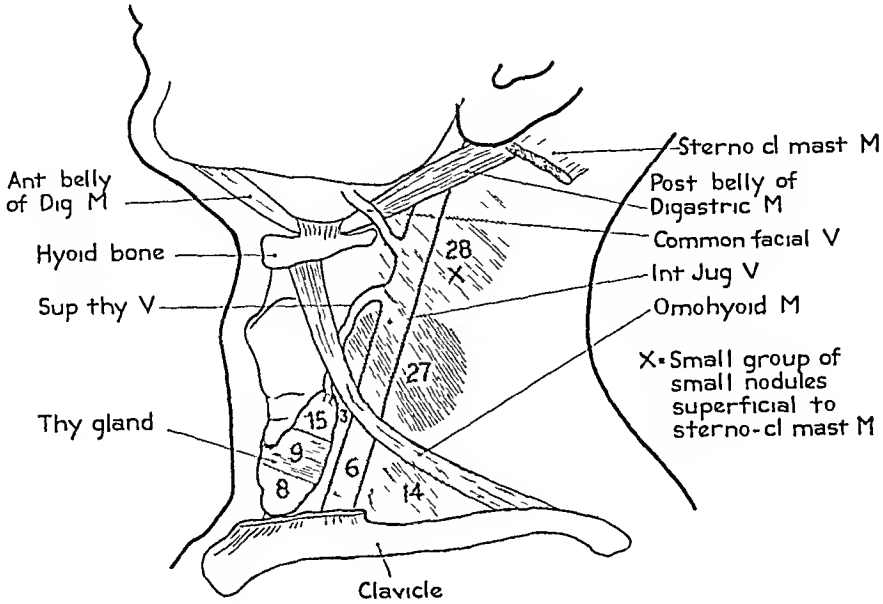


FIG 4—Diagram showing a composite view of the location of all of the nodules or groups of nodules in all of our cases, as if all were in the left side of the neck.

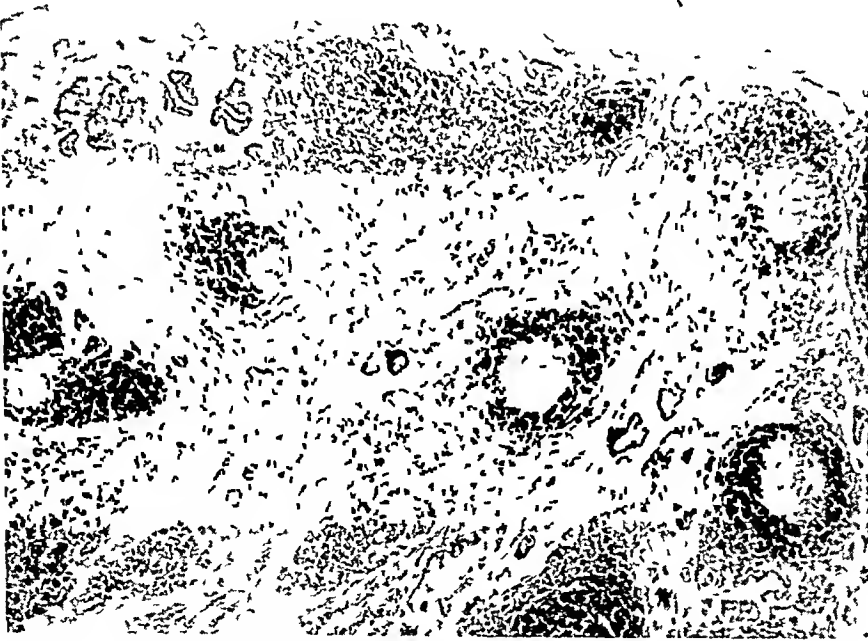


FIG 5—Photomicrograph from a case of papillary carcinoma of the main thyroid (with no lateral aberrant thyroid), showing multiple metastatic foci of papillary tumor scattered through a lymph node.

The upper deep cervical region, above the omohyoid muscle, (2) the lower deep cervical region, below the omohyoid muscle, (3) the supraclavicular region.

As we have said above, the malignancy of these tumors of lateral aberrant thyroids has been a matter of difference of opinion. In the literature we

were able to find only eight deaths reported—two by Dunhill (1931), one by Crile (1939), three by Waid (1940), and two by Lahey (1940). In only one of these was there definite evidence of distant metastases. Un-



FIG. 6—Photomicrograph of another lymph node from the same case as Figure 5 showing tumor in the afferent lymph vessel and in the marginal sinus

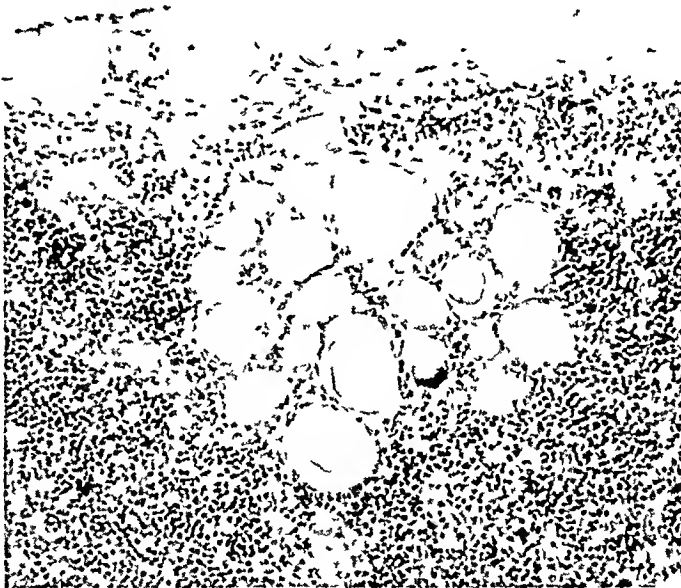


FIG. 7—Case 1 Photomicrograph showing aberrant thyroid tissue in a lymph node

fortunately, however, the majority of the reported cases lack follow-up data, and we wish later to emphasize that this is essential in order to determine the true nature of these tumors.

The distinction between lateral aberrant thyroid tumors and metastases to cervical lymph nodes from carcinoma of the thyroid is always difficult and at times impossible. In all our cases we have accepted metastases only when

groups of tumor cells lie scattered in a structure which has the architecture of a lymph node, *i e*, marginal sinus, sinusoids and lymph follicles. In Figures 5 and 6 the photomicrographs show such a metastasis, with papillary tumor not only in the marginal sinus and scattered through the sinusoids, but also in the afferent vessel leading to the node. Figure 7 from Case 1 shows what we consider aberrant thyroid tissue not occurring separately but situated in a lymph node. This being the case, if such a structure became neoplastic it would obviously be exceedingly difficult—really impossible—to differentiate between a primary tumor in a lymph node and a metastasis. Likewise, it is equally impossible to be certain whether an encapsulated nodule is a primary tumor, or a metastasis in a lymph node which has destroyed all the lymph node architecture. But we feel that multiple small foci in a lymph node are much more likely to represent metastases than to be multiple aberrant foci. Case 26 illustrates multiple aberrant thyroid nodules, bilateral, and also metastases.

The considerable number of cases recently reported attests the better recognition of the disease. Guegei (1876) states that in autopsy material a careful examination reveals aberrant thyroid tissue in 10 per cent of all cases. We know of no report since then in which the actual incidence of the anomaly is given. Lahey (1940) reports 36 cases of lateral aberrant thyroid carcinoma in 18,600 goiter operations at the Lahey Clinic, an incidence of approximately 0.2 per cent, and Cile, reporting the same series earlier gave an incidence of one lateral aberrant thyroid to 1,000 goiter operations. This undoubtedly includes the benign cases.

In a total of approximately 3,800 surgical thyroid specimens at the Presbyterian Hospital, from 1924 to January 1, 1941, of which 109 were carcinomas, we are presenting 30 cases of lateral aberrant thyroids. These, even if the main gland was also involved, are not included in the figure for the carcinomas given above. There were in this period also six cases of median aberrant thyroid tumors, and in the same period 39 thyroglossal cysts.

The difficulty in diagnosis reported in the literature has been present in our series. The commonest clinical picture is that of enlarged cervical lymph nodes. The following disease entities are, therefore, difficult to differentiate from lateral aberrant thyroids: Chronic lymphadenitis, tuberculous lymphadenitis, Hodgkin's disease, lymphosarcoma, metastatic carcinoma. Branchial cyst and carotid body tumor have also been confused. Even when the masses are exposed at operation the diagnosis may not be suspected unless they are strikingly bluish-black due to hemorrhage, which often occurs in the papillary tumors, or reddish enough to suggest normal thyroid tissue.

Our 30 cases have been classified as follows:

The six cases classified as adenocarcinoma all showed large undifferentiated areas, and two of them showed very striking spindle cell metaplasia.

It is not possible in the space allotted to analyze the case histories in detail. We regret this because we would like to present all the evidence upon which the diagnoses are based, realizing the controversial nature of this

material We have scrutinized repeatedly the clinical, anatomic and pathologic features, and discarded all cases in which there could be any doubt as to the aberrant nature of the tissue Summaries of the essential findings appear in the tables

TABLE I

	No of Cases
<i>Benign</i>	
Lateral aberrant thyroid gland	2
Nontoxic nodular goiter of lateral aberrant thyroid	1
Adenoma of lateral aberrant thyroid gland	1
Papillary cysto adenoma of lateral aberrant thyroid	3
	—
	7 (3 not neoplasms)
<i>Malignant</i>	
Papillary carcinoma of lateral aberrant thyroid (thyroid involve- ment in all but three)	12
Papillary and adenoma malignum type combined (both with thyroid involvement)	2
Adenoma malignum type with no marked papillary arrangement (two with thyroid involvement and one without)	3
Adenocarcinoma (thyroid involvement in four)	6
	—
	23 (12 predominantly papillary)

Table II summarizes the first three cases of the series which we do not regard as neoplasms The first two are simple thyroid tissue without abnormality other than site, and were not recognized clinically or grossly, but were found on microscopic examination Case 1 is illustrated in Figure 7 Case 2, as will be seen from the table, showed none of the histologic evidences of toxicity demonstrated in the main gland Case 3 showed the same involutional changes in the aberrant nodule as, 11 years previously, were found in the main gland Multiple lateral nodules had appeared in this case eight and one-half years after thyroidectomy, and one was removed for diagnosis The remaining nodules have not changed clinically, but it has been decided to remove these in the near future because of the high incidence of neoplasm in these lateral masses

TABLE II
LATERAL ABERRANT THYROID

Case No	Age	Sex	Dura- tion	Loca- tion	No of Nodules	Condition of Thyroid Gland	Pathology	Treat- ment	Result
1	42	F	?	? side	1	Nontoxic nodular goiter	Lat aberrant thyroid tis- sue in lymph node	Excision	No recurrence 13 mos
2	54	F	?	? side	2	Toxic nodu- lar goiter	Lat aberrant thyroid tissue	Excision	No recurrence 75 mos
3	25	F	2 yrs	Left	1	Thyroid- ectomy 11 yrs prev for nontoxic nodular goiter	Nontoxic goiter lat aberrant thyroid	Biopsy	Persistence of nodules not removed 17 mos These to be re- moved

Table III is the analysis of the four cases thought to be benign neoplasms. Two cases originally included in this group are now classified as malignant, because recent operations for recurrence have demonstrated tumors, which, while still architecturally similar to the original growths, now have clear cut

FIG 8



FIG 9

FIG 8—Case 6 Photomicrograph of a benign papillary cystadenoma. This came from a single encapsulated mass. The patient is well, 52 months after operation.

FIG 9—Case 10 Photomicrograph of a papillary carcinoma of lateral aberrant thyroid. The main thyroid was involved in this case.

blood vessel invasion. One of these has been followed 11 years since the first procedure.

It is not impossible that a longer follow-up will prove us wrong on these four cases. The burden of proof is on the pathologist who calls any of these tumors benign. One must study the character of the cells, observe any nuclear

variation, search painstakingly for blood vessel and capsule invasion, and evaluate all these factors. Figure 8, Case 6, illustrates the histologic picture of a papillary cysto-adenoma which had only one excision, and no recurrence at 52 months. Case 4 of this group had had two previous operations for similar tumor, and Case 7 one previous operation. In neither of these cases was tumor found in the main gland, although Case 7 had a nontoxic nodular goiter. This case is the only one without a long follow-up, and has a persistent nodule which is to be removed shortly.

TABLE III

BENIGN TUMORS OF LATERAL ABERRANT THYROID									
Case No	Age	Sex	Duration	Location	No of Nodules	Condition of Thyroid Gland	Pathology	Treatment	Result
4	52	F	18 yrs	Right	1	Not enlarged	Adenoma lat ab thy	Excision	No recurrence 108 mos
5	48	F	13 yrs 2 previous excisions elsewhere	Left	1	Not enlarged	Pap cysto-adenoma lat ab thy	Excision	No recurrence 101 mos
6	53	F	9 yrs	Left	1	Not enlarged	Pap cysto-adenoma lat ab thy	Excision	No recurrence 52 mos
7	40	F	7 yrs 1 previous excision	Right	4	Nontoxic nod goiter	Pap cysto-adenoma lat ab thy	Excision	Persistent nodule 7 mos To be removed

Table IV is the analysis of 12 cases of tumor thought to be malignant, and predominantly papillary. In these 12 cases the thyroid itself was involved in all but three, but in eight of the 12 the presenting symptom was the lateral mass. Two cases were bilateral, and these both had thyroid involvement. They were exceedingly well differentiated tumors, and this was striking in Case 10 (Fig 9), where the metastasis in the lung (Fig 10) has a most innocent appearance, reproducing the well-differentiated papillary character of the original growth. Presumably Cile would not classify any of these as papillary carcinoma for he states that "A tumor which shows invasion of the blood vessels is here classified as a malignant adenoma even though it contains papillary areas," and "Invasion of blood vessels is rarely seen in tumors that are predominantly papillary." Much depends, of course, on one's interpretation of the word "predominantly," but in this group many sections were made of the tissue and the papillary arrangement was everywhere striking, even in the blood vessels (Fig 11). Colloid was present in all but one of the tumors (this case had only a small biopsy) and psammomatous bodies in nine of the 11. Blood vessel invasion was twice not demonstrated. The material in the first of these was scanty, but the patient, Case 29, died of lung metastases. The other case without blood vessel invasion demonstrated is too recent to evaluate, having lived only 40 months after operation,

although still free from evidence of disease In two the thyroid was not involved, and one of these, Case 29, already cited, died of local disease with

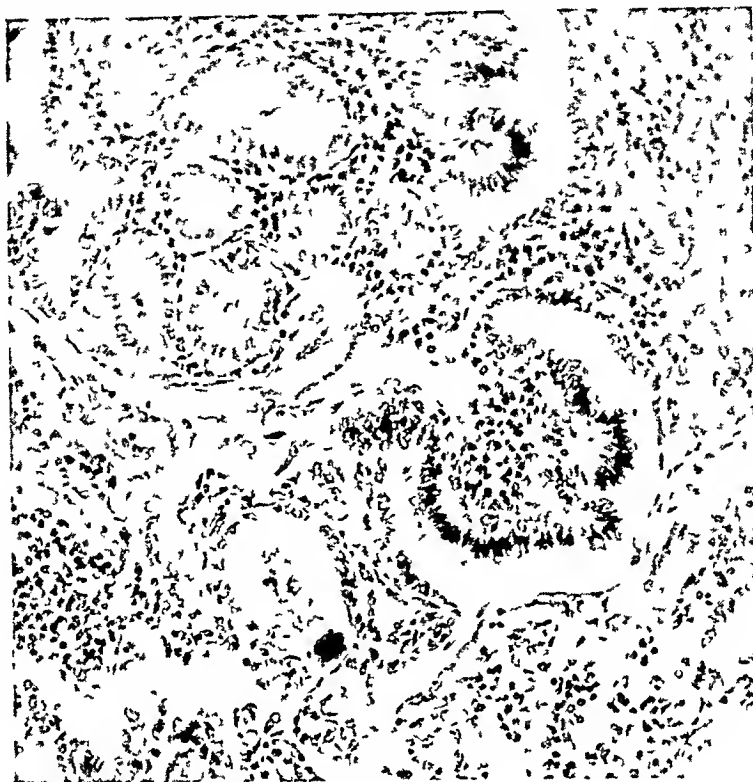


FIG 10 —Case 10 Photomicrograph, high power, of lung metastasis, showing well differentiated papillary tumor (Section through the courtesy of Mt Sinai Hospital)

roentgenographic evidence of lung metastases, while the other, Case 9, has persistent local disease and roentgenographic evidence of pulmonary metastases



FIG 11 —Case 15 Photomicrograph showing blood vessel invasion by well differentiated papillary tumor

Four of the cases had what we interpreted as lymph node metastases in addition to the aberrant nodules One is dead This is Case 10, with dis-

tant metastases demonstrated at autopsy. The other three are living (Cases 14, 15 and 16), one month, 24 months, and one month after their last operative procedures. All the cases with lymph node involvement showed blood vessel invasion.

Radiotherapy was employed in all four of the fatal cases—radium pack, radium needles and roentgenotherapy in the first, roentgenotherapy in the second and third, and radium needles and roentgenotherapy in the fourth. There was slight regression of the tumor in each case, but no arrest. One patient, who is still living, was treated intensively with roentgen-ray, a total of 13,240 r to six fields before operation, with some regression at first. This case, No. 14, has required extensive surgery since then, and may well require more. One case, No. 9, had intensive radiation after biopsy, with temporary regression, but with recent increase in the size of the mass, and has recent roentgenographic evidence of lung metastases. Two other cases, Nos. 13 and 17, received intensive radiation after removal of the tumor. The effect of roentgenotherapy in these, therefore, cannot be judged, and they only have a short follow-up, but they are living without evidence of disease 40 and 12 months, respectively, after the last operation.

Table V is the analysis of 11 cases of malignant tumors not predominantly papillary. These are subdivided somewhat according to histologic appearance in Table II.

The first two cases, Nos. 20 and 21, were partly papillary, and also had large adenomatous areas resembling simple adenoma more than adenocarcinoma, or what we would call "carcinoma, adenoma malignum-type." One is living without evidence of disease 28 months after the second operation, and one without disease seven months after the third operation. Both showed some colloid acini. Both had blood vessel invasion. Neither had lymph node invasion. In both, the main gland was also involved. Both had radical surgery and radiation, the first had radiation before operation without effect, the second after removal of tumor, but a new nodule appeared during treatment.

The next three cases, Nos. 22, 23, and 24, were carcinoma, adenoma malignum-type, two with no papillary arrangement at all, and one with a very little. All showed colloid follicles. All had blood vessel invasion but no demonstrated lymph node metastases. One, Case 22, was radiated for recurrence and showed some regression but died with local disease. Case 24 lived 70 months, having had no postoperative radiation, and died without local recurrence but with roentgenographic evidence of metastases in vertebrae and lungs. This case was originally erroneously classified as simple adenoma.

Case 23 was originally classified as a simple adenoma, but was always under suspicion because she had a nodule in the main gland. This case had been followed for nearly 11 years after the first operation (she had a five-year history of tumor before operation), and her very recent exploration yielded a good-sized tumor still lateral, with marked blood vessel invasion.

The next six cases are arranged in order, as far as possible, according to the histologic evidence of differentiation. The first, No. 25 (Fig. 12), and

TABLE IV

MALIGNANT TUMORS OF LATERAL ABERRANT THYROID—PREDOMINANTLY PAPILLARY

Case No	Age	Sex	Dura- tion	Location	No of Nodules	Condition of Thyroid Gland	Lateral Neck Pathology	Treatment	Result
8	30	F	18 mos	Right	5	Not enlarged	Pap carc of lat ab thyroid	Excision later	Living without evidence of dis- ease 19 mos after 1st op , 2 wks after 2nd op Living with local disease and lung met 38 mos
9	63	F	24 mos	Left	Several	Not enlarged	Pap carc of lat ab thyroid	Biopsy X-ray	Died lung and cerebral met 111 mos after 1st op
10	61	F	6 mos	Left	2 (3 lymph nodes)	Papillary carcinoma	Pap carc of lat ab thyroid Met to lymph nodes	Excision, thyroidectomy and radium	Died lung met 38 mos
11	30	F	14 mos	Left	11	Papillary carcinoma	Pap carc of lat ab thyroid	Excision	No recurrence 64 mos
12	40	M	6 mos	Right	1	Not enlarged	Pap carc of lat ab thyroid	Curettage and x-ray	Died 5 mos , with lung metas- tases
13	25	F	5 yrs	Right	6	Papillary carcinoma	Pap carc of lat ab thyroid	Excision, thyroidectomy, and x-ray	No recurrence 40 mos
14	21	M	2 wks	Bilateral	19	Papillary carcinoma	Pap carc of lat ab thyroid Met to lymph nodes	Excision, thyroidectomy and x-ray	No recur 39 mos after 1st op 1 mo after 5th op
15	17	M	1 yr	Left	7	Papillary carcinoma	Pap carc of lat ab thyroid Met to lymph nodes	Radical neck dissection Thy- roidectomy	No recur 25 mos after 1st op, 24 mos after 2nd op
16	24	F	20 mos	Bilateral	24	Papillary carcinoma	Pap carc of lat ab thyroid Met to lymph nodes	Bilat radical dissection and thy- roidectomy Exc recurrent nodule	No recur 12 mos after 1st op, 1 mo after 2nd op
17	42	F	8 mos	Right	2	Papillary carcinoma	Pap carc of lat ab thyroid	Excision, thyroidectomy x-ray	No recurrence 12 mos
18	50	M	6 mos	Right	Several	Papillary carcinoma	Pap carc of lat ab thyroid	Biopsy Partial thyroidectomy, x-ray	Died 8 mos , local disease
19	47	F	12 mos	Right	Several	Papillary carcinoma	Pap carc of lat ab thyroid	Biopsy Partial thyroidectomy, radium and x-ray	Died 6 mos , local disease

thought least undifferentiated, is dead of local disease. In this case the thyroid was not involved, and no blood vessel invasion was demonstrated, lymph node invasion, however, was seen. Roentgenotherapy caused only slight regression at first. Radical neck dissection also failed to control the disease.

The next case, No. 26, is the only child in the series. This case has already been published *in extenso* (Langman and Bruch) as a carcinoma with bilateral metastases. On reanalysis, however, we believe that, in addition, it represents

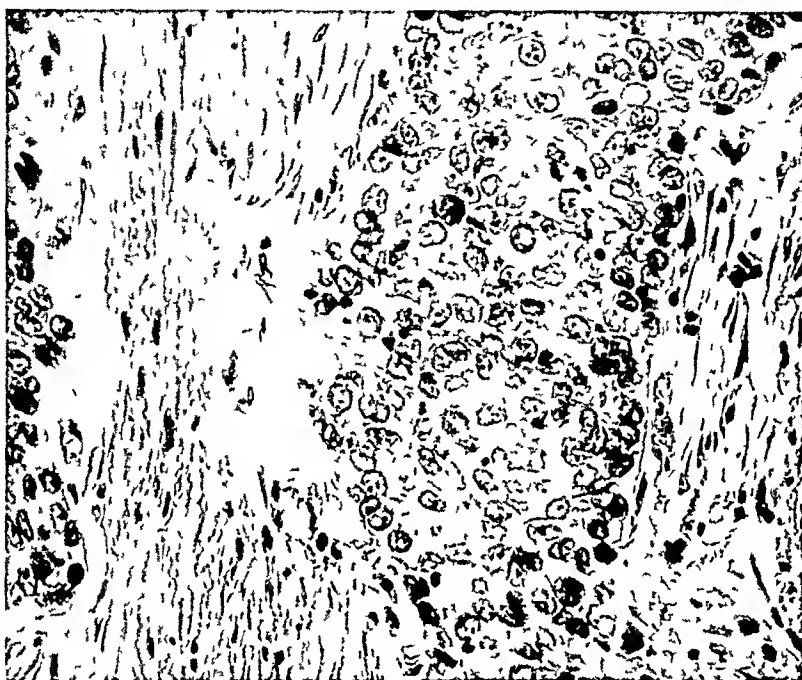


FIG. 12.—Case 25. Photomicrograph of biopsy specimen which was erroneously interpreted as squamous cell epithelioma.

bilateral carcinoma of aberrant thyroid, and as such, with a longer follow-up, should be included here. The disease in this child was very extensive, and was treated by radical surgery and postoperative radiation. She had a total thyroidectomy, bilateral radical neck dissection, and required thyroid extract, but it is of interest that she no longer requires this, suggesting that some thyroid tissue still remains. She is free from evidence of disease after 60 months.

Of the last four cases, one, Case 29, is dead with roentgenographic evidence of lung metastases, one, Case 27, is living with questionable recurrence locally, after 24 months, and two are living without evidence of disease, one, 118 months, and one, 28 months after their second operations, and one, 111 months. The one, Case 28, living 118 months, who was thought to have a highly malignant tumor (Fig. 13) had a biopsy, and three years later (because he failed to return for treatment) a partial thyroidectomy and excision of the lateral mass. Recurrence appeared after roentgenotherapy (6,000 r), and was then apparently not controlled by insertion of needles (2,710 mg. hr.), so this was

TABLE V
MALIGNANT TUMORS OF LATERAL ABERRANT THYROID—NOT PREDOMINANTLY PAPILLARY

Case No	Age	Sex	Dura- tion	Location	No of Nodules	Condition of Thyroid Gland	Lateral Neck Pathology	Treatment	Result
20	60	M	12 mos	Left	1	Carcinoma	Carc lat ab thy Pap and ad malign- type combined	(1) Part thyroidectomy and excision (2) Excision X-ray	No recur or disease 38 mos after 1st op 28 mos after 2nd op
21	35	F	9 yrs	Bilateral	6	Carcinoma	Carc lat ab thy Pap and ad malign- type combined	Left rad dissect Thyroidec- tomy X-ray Excision Ra- dium pack X-ray (1) Part thyroidectomy (2) Excision	No recur 16 mos after 1st op, 7 mos after 3rd op
22	69	F	25 yrs	Left	1	Carcinoma	Carc ad malign-type lat ab thy (later primary ca breast)	(1) Part thyroidectomy (2) Excision	Dead with local disease 92 mos
23	16	F	5 yrs	Bilateral	9	Adenoma	Carc lat ab thy, ad malign-type	Excision Partial thyroidec- tomy Exc Recurrence	No recurrence 129 mos after 1st op, 1 mo after 3rd op
24	59	F	35 yrs	Right	6	Not enlarged	Carc lat ab thy, ad malign-type	Excision	Died 94 mos Met to spine lung
25	50	F	12 mos	Left	3	Not enlarged	Carc lat ab thy Met to lymph nodes	Left rad dissect X-ray	Died 5 mos local disease
26	4	F	2 mos	Bilateral	7 and many small	Carcinoma	Carc lat ab thy Met to lymph nodes	In stages Bilat rad dissect Thyroidectomy, total X-ray	No recur 60 mos
27	47	F	?	Right	2	Carcinoma	Carc lat ab thy	Thyroidectomy Excision X-ray	? recurrence 24 mos
28	50	M	11 yrs	Right	1	Carcinoma	Carc lat ab thy	Excision Thyroidectomy X-ray plus radium	No recur 118 mos
29	40	F	7 yrs	Left	4	Carcinoma	Carc lat ab thy	(1) Part thyroidectomy (2) Excision	Died 16 mos, local disease Lung met
30	23	F	24 mos	Right	4	Not enlarged	Carc lat ab thy Met to lymph nodes	Excision X-ray	No recur 38 mos after 1st op 28 mos after 2nd op

followed by a radium pack of 25,000 mg hr. Disease persisted and roentgenotherapy was again employed, and, with 5,100 r, the disease has appeared to be under control for the last seven years. This is the only case in the series which strongly suggests the roentgenotherapy has altered the course of the disease*.

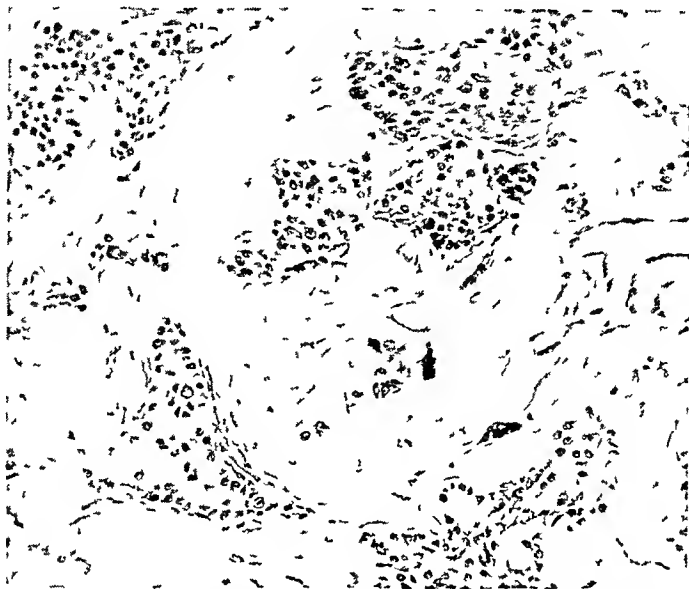


FIG 13—Case 28. Photomicrograph showing undifferentiated carcinoma with much fibrosis. This patient is well 111 months after operation and roentgenotherapy for recurrence. He gave a history of tumor for 11 years before operation.

Discussion—The group of benign cases is so small that no separate statistical summary is of interest. Certain findings may be stressed in the 23 malignant cases taken as a group.

There were 17 females and six males, a ratio of 2.8 to 1. There were four Negroes in the group.

The age on onset varied from four to 61. By decades the distribution is shown in Table VI.

TABLE VI
AGE OF ONSET BY DECADES

Decades	No of Cases
1-10	1
11-20	2
21-30	8
31-40	3
41-50	6
51-60	1
61-70	2
Total	23

The basal metabolic rate was often not determined, and never of significance, except postoperatively in the one case with total thyroidectomy. There was no case of hyperthyroidism in the malignant group.

* The factors for roentgenotherapy were constant for all the cases. These were as follows: 200 K V, 25 M amps, 50 cm T S D, with 1.05 mm Cu and 1.25 mm Al. The single dose varied from 100 to 125 r.

In the malignant cases the presenting symptom was the lateral mass in 15, or 65 per cent. In this same group the thyroid gland was involved in 17 cases, or 74 per cent.

The malignant cases in which the thyroid was uninvolved are as follows

- (1) Papillary carcinoma. Dead, with persisting local disease and roentgenographic evidence of lung metastases.
- (2) Papillary carcinoma. Living, with local disease and roentgenographic evidence of lung metastases.
- (3) Papillary carcinoma. Living, without evidence of disease, 19 months after the first operation, two weeks after the second.
- (4) Adenoma malignum. Dead, 94 months after operation, with no local recurrence but with roentgenographic evidence of metastases to vertebrae and lungs.
- (5) Adenocarcinoma. Dead, five months after operation, of local disease.
- (6) Adenocarcinoma. Living, without evidence of disease, 28 months after the second operation.

Lymph node involvement occurred in seven cases, or 30 per cent. In our series of 109 cases of carcinoma of the main gland there have been only four cases of regional lymph node metastases without lateral aberrant thyroid disease. Of these four cases, one is living without evidence of disease 63 months after partial thyroidectomy and excision of the metastatic nodes. This patient had a recurrence which has disappeared under roentgenotherapy. The other three all have persisting disease, six months, 64 months and 133 months, respectively. The patient who is living, without evidence of disease, may have had the course of the disease altered by roentgenotherapy, as this is at least a five-year arrest.

The statistics in the tables concerning the duration of the disease before and after operation should be noted carefully. It is obvious from these figures that long duration before, and *even after operation* is not necessarily an indication that the patient will not eventually succumb to the disease.

CONCLUSIONS

From this series we feel that it is evident that, even with careful laboratory study, it is difficult to differentiate between benign and malignant tumors in lateral aberrant thyroids. For this reason we advocate biopsy of one or more nodules with subsequent therapy dependent upon the laboratory report. If the biopsy shows a benign lesion, then an operation to remove all of the nodules is advised, because of the number of cases which give such a long history of stationary masses which subsequently proved to be carcinoma. It is, of course, impossible to know whether the histologic picture in these was the same from the onset of the swellings.

If the biopsy shows malignant disease with or without lymph node involvement, a radical neck dissection is advisable, on both sides if the disease is

bilateral If the thyroid gland is involved, a partial or complete thyroidectomy is indicated, depending upon the findings

There is not enough evidence to evaluate the effect of roentgenotherapy, but in at least two patients the disease appears to have been arrested by it. In others, recurrences appeared during treatment. It seems, therefore, a matter for personal decision in each individual case. It is the only therapeutic measure in the cases which, for one reason or another, are considered inoperable.

Finally, from the study of this series we feel justified in stating, emphatically, that all of these tumors should be considered potentially malignant, studied with care, treated radically, and followed indefinitely.

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MASKED HYPERTHYROIDISM^{*}

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GENERALLY SPEAKING, the diagnosis of frank hyperthyroidism of the exophthalmic type or the type associated with toxic adenoma of the thyroid gland, offers no particular difficulty. There are, however, patients suffering from thyrotoxicosis in whom the classic signs and symptoms of hyperthyroidism are either wanting or are not obvious. Such a person presents an atypical clinical picture of some other type of disease, such as organic heart disease accompanied by congestive heart failure, angina pectoris or auricular fibrillation, arterial hypertension, diabetes mellitus, gastro-intestinal disturbances, some form of malignancy, chronic pulmonary tuberculosis, psychoneurosis or some muscular disease. In these instances the thyrotoxicosis is either undiagnosed or diagnosed very late.

Marie,¹ as early as 1883, was perhaps the first to call attention to atypical hyperthyroidism. He stressed the importance of recognizing Basedow's disease with tremor and moderate tachycardia but without exophthalmos or goiter.

In 1885 Charcot,² under the caption "*Maladie de Basedow formes frustes*," drew attention to those cases of exophthalmic goiter in which one or the other of the triad of symptoms, struma, exophthalmos and tachycardia, was wanting. In 1889, he further elaborated upon cases of hyperthyroidism which failed to present the leading symptoms and labeled them as the attenuated form of the disease.

Levine and Sturgis,³ in 1924, under the title "Hyperthyroidism Masked as Heart Disease," described five cases with symptoms referable to the heart, usually palpitation, pain, dyspnea and transient attacks of auricular fibrillation. Boas and Shapiro,⁴ in 1925, discussed a group of cases of hyperthyroidism with hypertension which they regarded as a special syndrome to be distinguished from the ordinary form of hypertension and from exophthalmic goiter. Their patients showed an elevation of both the systolic and diastolic blood pressures, associated with cardiac hypertrophy. Hubbell,⁵ in 1927, recorded two cases simulating diabetes mellitus. Levine and Walker,⁶ in 1929, stressed the importance of recognizing latent hyperthyroidism in cases of auricular fibrillation which fail to respond to digitalis therapy. They mentioned also the fact that some of their patients with masked hyperthyroidism showed a transient glycosuria, mild persistent glycosuria, or an appreciable hypertension.

Hamburger and Lev,⁷ in 1930, reported five cases of masked hyperthyroidism and reviewed the subject in a very comprehensive manner.

^{*} Read before the New York Surgical Society, April 9, 1941.

They noted that their patients were all at or beyond the middle decade of life and that they did not present the usual obvious signs and symptoms of toxic goiter. The classical features of the disease were replaced by apathy, weakness, loss of weight, pigmentation, early fatigue, and some slight staring expression of the eyes, and in many instances by the clinical picture of some circulatory disorder, namely, congestive heart failure, auricular fibrillation, tachycardia, or angina pectoris. A lesser number presented the clinical picture of diabetes mellitus or of pernicious hyperemesis. Veibrycke,⁸ in 1931, reported a series of 34 cases of hyperthyroidism masquerading as some form of gastro-intestinal disease. In 1931 and 1932, Lahey^{9, 10, 11, 12} contributed an important series of papers on the subject. He called particular attention to an atypical form of the disease occurring in middle-aged or past middle-aged individuals, which he termed "apathetic hyperthyroidism."

Shorr¹³ recently observed a group of cases of hyperthyroidism simulating myasthenia gravis or progressive muscular dystrophy. He emphasized that the muscular weakness in thyrotoxicosis, as well as in the muscular diseases, is the result of a defective creatine metabolism. In all these conditions creatine is excreted in abnormal amounts in the urine. However, by the use of iodine the creatine defect can be abolished in Graves' disease but not in muscular dystrophy or myasthenia gravis. Furthermore, the creatinuria of thyrotoxicosis is completely controlled following thyroidectomy.

It has seemed to us worth while to call attention again to the so-called masked hyperthyroidism, since the diagnosis of this form of the disease not infrequently passes unrecognized.

CASE REPORTS

Case 1—A F, male, age 60, was seen for the first time February 25, 1939. His main complaints were weakness, considerable loss of weight, precordial pain, and dyspnea on exertion. These symptoms began about a year and a half ago and became progressively more marked. The weakness progressed to the stage where he found it difficult to walk without tiring readily. He lost about 12 lbs. in the past three months.

His past history showed that he had been a diabetic of moderate severity for many years.

Examination showed the patient to be thin, almost emaciated, weighing 114 lbs. There was no exophthalmos. The neck was not enlarged and there was no evidence of an enlarged thyroid gland. The lungs were clear. The heart was not enlarged to percussion, but it had a rate of 116 to 120. There was also a short systolic murmur at the apex. Blood pressure 155/60. The abdomen and the extremities showed no abnormal findings. The reflexes were normal.

Gastro-intestinal and chest roentgenograms were entirely negative. The electrocardiogram did not show any remarkable changes. The urine showed a trace of sugar. The blood sugar was 155 and the cholesterol 250 mg. per cent. The blood CO₂ combining power was 54.1 per cent.

It was our impression that we were dealing here with a case of masked hyperthyroidism, i.e., the hyperthyroidism was masquerading as a cardiac and/or some form of malignancy.

A basal metabolism determination was then made, which showed plus 50.

The patient was put to bed and given a high carbohydrate diet and insulin. He also received Lugol's solution, 10 minims three times a day. Within a relatively short time

he showed definite improvement. He began to gain weight and felt stronger. There was also a slowing of his heart rate with cessation of the precordial pain.

On May 23, 1939 he had a subtotal thyroidectomy performed. The pathologic diagnosis was that of colloid goiter suggesting the stage of regression in response to iodine therapy. Suggestion of previous toxicity was seen in one lobe.

The operation was followed almost immediately by very rapid and progressive improvement in his condition.

Examination on June 26 showed him to appear well nourished, with a weight of 138. His heart rate was 78. His blood pressure, however, remained elevated at 170/80. His diabetes was well under control. His basal metabolic rate was now plus 3. He had a sense of general well-being, and was entirely free from any symptoms. His present weight is 148.

Comment—In this patient the outstanding symptoms were progressive weakness and loss of weight, precordial pain, and dyspnea. On examination there were none of the striking signs of hyperthyroidism except perhaps for a moderate tachycardia. He was for a long time considered to be a diabetic, complicated by coronary artery disease. Later in the course of his disease, in view of his persistent weight-loss, some form of malignancy was suspected. This was ruled out by radiographic studies. Indeed, the progressive asthenia and weight-loss in addition to the moderate tachycardia led to the diagnosis of hyperthyroidism. This was subsequently confirmed by the high basal metabolic rate and the therapeutic response to iodine medication. Following thyroidectomy, there was a complete recovery.

Case 2—E. S., female, age 36, was admitted to Bellevue Hospital, March 31, 1939, with a complaint of "thumping of the heart" of two weeks' duration. The attacks would come on suddenly and were accompanied by cold sweats and a feeling of precordial discomfort. The episodes were usually of short duration. There was no dyspnea, cough or frank cardiac pain.

Her past history showed that she had had hypertension for about eight years. On several occasions she had symptoms referable to the hypertension, such as vertigo, headaches, vision disturbances, and epistaxis.

Physical examination showed the patient to be moderately pale and somewhat apprehensive. Her weight was 99 lbs. Temperature 100° F, pulse 140, respirations 20. There was no exophthalmos. The thyroid gland appeared palpable but not significantly enlarged. The lungs were clear. The heart was slightly enlarged, had a ringing aortic second sound and a rapid gallop rhythm. There were no murmurs. The heart rate could not be modified by pressure on either carotid sinus. Blood pressure 220/140. There was no tremor of the hands. The fundus examination showed moderately advanced hypertensive vascular changes.

The diagnosis on admission was essential hypertension and hypertensive heart disease. It could not be definitely determined, clinically, what form of tachycardia the patient had.

Several electrocardiograms were taken. Some showed runs of paroxysmal tachycardia of auricular origin but the majority showed a sinus tachycardia. Other changes noted in the tracings were depression of R-T 1 and 2 and inversion of T 1 and 2. Thus, there was evidence of some myocardial damage.

Several urine examinations were negative except for an occasional trace of albumin and a moderately low specific gravity. The blood chemistry was essentially normal. A roentgenogram showed the heart to be obliquely oval and the size and shape to be within normal limits. Roentgenograms of the kidneys did not show any evidence of calculi or of polycystic disease.

An attempt was made to control the tachycardia with digitalis, quinidine and also

ipecac, but without any success. The possibility of hyperthyroidism was, therefore, entertained. Several basal metabolism tests were then made and the readings ranged between plus 52 to plus 82.

It was our impression, therefore, that the patient had a masked form of hyperthyroidism associated with essential hypertension. She was, therefore, placed on a high caloric diet and Lugol's solution. On this regimen the patient showed some degree of improvement.

On June 1, 1939, under cyclopiopane anesthesia, a subtotal thyroidectomy was performed.

The pathologic report on the removed thyroid gland was that of mild epithelial hyperplasia.

She had an uneventful convalescence and showed rapid, progressive improvement. Her heart rate became normal and has remained so. She has also gained 14 lbs. in weight. The basal metabolic rate was reduced to plus 0.9. Her hypertension, however, has persisted, although somewhat reduced.

Comment—This patient on admission appeared to be a definite case of essential hypertension associated with hypertensive cardiopathy. The tachycardia, with symptoms referable to it, appeared to be one of the paroxysmal forms. There was nothing on admission to lead us to suspect the presence of an obscure thyroid disturbance. However, when the tachycardia failed to respond to medication, the presence of an underlying hyperthyroidism was suspected. This was confirmed by the repeated high basal metabolism rates. While following the Lugol regimen there was only slight improvement, the postoperative progress was rapid and most satisfactory. It is to be noted, however, that the hypertension persisted. This was attributed to the presence of an irreversible diffuse vascular disease. In this connection it will be recalled that Boas and Shapiro,⁴ in 1925, reported a series of five cases presenting a diastolic hypertension with increased metabolism rate and concluded that such cases constituted a special syndrome.

Case 3—A S, female, age 59, was admitted to Sydenham Hospital, December 20, 1939, complaining of anorexia, flatulence, cardiac palpitation, nervousness, weakness, weight-loss, occasional dyspnea, slight swelling of the ankles, pain in the legs and arms and occasional sweating of the hands. These symptoms have lasted with remissions for more than five years and have become more pronounced and almost continuous during the past 10 days.

On examination, the patient appeared undernourished and apathetic. Her weight was 120 lbs. There was no exophthalmos and also the eye signs were negative. There was a slight enlargement of the left lobe and isthmus of the thyroid gland. There were a few moist and subcrepitant râles over the bases of both lungs. The heart was not enlarged and showed an irregular rhythm but no murmurs. The liver was felt one finger's-breadth below the costal border on the right side. The blood pressure was 200/60. There was a low-grade fever ranging between 99° and 101.6° F.

Examination of the urine showed a specific gravity of 1.012, a heavy trace of albumin and an occasional hyalin and granular cast. The phenolsulphonephthalein excretion was 15.5% in 2 hours. The blood urea was 17.5, and the cholesterol was 136 mg. per cent. The blood albumin was 3.9 and the globulin 2.6 Gm. per cent. A roentgenogram of the chest showed a generalized increase in the pulmonic markings and a heart of normal size. The electrocardiogram showed a QRS of low voltage and somewhat bizarre in the third lead, a depressed ST 4 segment, an inverted T 3 and auricular fibrillation. The basal metabolic rate was plus 7.1.

A diagnosis of hyperthyroidism was made and the patient was prepared for operation. On January 6, 1940, a left total thyroidectomy was performed. Except for an attack of bronchitis, the patient's postoperative course was uneventful. The blood pressure dropped to 135/80. The basal metabolic rate, however, was still plus 45.

The pathologic report on the specimen removed at operation was "microfollicular nodular goiter with degenerative changes."

The patient was readmitted to the hospital, April 28, 1940, for the purpose of operating upon the right side. Her general condition at that time was quite good. Two days later, five-sixths of the right lobe of the thyroid gland was removed.

The pathologic report on this specimen was "colloid involution stage of the thyroid."

A follow-up examination, September 16, 1940, showed the patient to be in excellent condition. Her weight was now 146½ lbs. The heart showed a regular sinus rhythm and a rate of 78. Blood pressure 150/90. The basal metabolic rate was plus 6.

Comment—This patient was a typical example of the apathetic hyperthyroidism, as described by Lahey.⁹ The outstanding complaints were weakness and weight-loss and symptoms referable to her heart. She was distinctly undernourished, and appeared apathetic. There was auricular fibrillation associated with congestive heart failure. These symptoms did not respond to the usual measures. These facts suggested an underlying thyrotoxicosis. There was also evidence of impairment of her kidneys which was unrelated to her thyrotoxicosis. The marked improvement in her condition and the relief of symptoms following operation were striking.

Case 4—A. A., female, age 52, seen for the first time March 7, 1934, complained of cardiac palpitation, a "shaky feeling," shortness of breath and episodes of epigastric pain associated with vomiting of two years' duration. She was hospitalized several times during that period for purposes of observation but no definite diagnosis was established.

Physical examination showed a poorly nourished female, appearing apathetic. Weight 120 lbs. There was no exophthalmos. A small nodule was felt in the right lobe of the thyroid gland. The heart showed a slight enlargement to the left, a regular rhythm, and a rate of 96. Blood pressure 150/80. The lungs were clear. There was moderate tenderness in the epigastrium but no masses were felt. There was no tremor of the hands.

The basal metabolic rate was plus 38. A gastro-intestinal series, done previously, was reported to have shown hypermotility but no definite evidence of organic disease.

A diagnosis of hyperthyroidism was made and on March 3, a subtotal thyroidectomy was performed.

The removed specimen showed dilated acini lined by pale, cuboidal epithelium and filled with colloid. A few of the acini showed mild hyperplastic changes. In places, there was a mild lymphocytic infiltration.

Her recovery was uneventful, and she was discharged March 12, 1934.

She has been followed periodically during the past six years, during which period she has been in excellent health and entirely symptom-free. She has gained 24 lbs in weight. Her heart rate is 76, and the basal metabolic rate varies from minus 10 to plus 4. Her blood pressure has remained 150/80.

Comment—We considered this case also one of apathetic hyperthyroidism masquerading as a gastro-intestinal disease. There were, however, symptoms suggestive of impaired myocardial function. The persistent moderate tachycardia along with a small palpable nodule in the thyroid gland led us to suspect the possibility of a thyrotoxic factor. Except for the persistence of

the moderate hypertension, she has remained in excellent health following the operation

Case 5—M R, female, married, age 56, when seen on February 2, 1940, complained of "nervous stomach," gas eructations, a smothering sensation and fainting spells of two years' duration. There was also cardiac palpitation, and loss of 15 lbs in weight.

Examination revealed a poorly nourished female, appearing older than her age. Her weight was 111 lbs. The eyes were entirely normal. The neck showed an adenoma of about 2x3 cm in the left upper lobe of the thyroid gland, which had never been noticed by the patient. This was completely hidden under the sternocleidomastoid muscle. The heart was not enlarged, and showed a regular rate of 100, and a faint systolic murmur at the apex. The liver was felt one finger's-breadth below the costal margin. Blood pressure 140/70. There was no tremor of her hands or tongue.

The electrocardiogram showed a regular sinus rhythm, a rate of 110 and no other abnormalities. Urine. Specific gravity 1.024, a faint trace of albumin, and 0.3% sugar. The basal metabolic rate was plus 26.

The moderate tachycardia, the weight-loss, and the presence of a small thyroid nodule suggested the diagnosis of thyrotoxicosis. Following the usual preoperative treatment, a subtotal thyroidectomy was performed on February 23.

The pathologic report showed a hyperplastic thyroid with colloid changes, probably due to iodine medication.

She made an uneventful recovery. At the time of her discharge on February 29, her weight was 120 lbs, the heart rate 78, and the basal metabolic rate minus 10.

A follow-up, May 31, 1940, showed the patient to be symptom-free. Weight was 128 lbs, heart rate 80. The blood pressure remained unchanged, and her urine has been sugar-free since operation. Her blood sugar was 150 mg per cent.

Comment—This poorly nourished and senile-appearing patient was an instance of hyperthyroidism masked as a case of diabetes mellitus associated with nervousness. The presence of hyperthyroidism was suggested by the moderate tachycardia, weight-loss, and a thyroid nodule. There was a complete reversal of her symptoms following proper therapy.

Case 6—S C, male, age 58, entered Bellevue Hospital, May 9, 1939, complaining of pain over his precordium and left chest in the region of the scapula, pain over the lower back, weakness and cardiac palpitation of two weeks' duration. These symptoms became progressively more marked.

Examination revealed a well-developed, well-nourished, middle aged man. There was no enlargement of the thyroid gland. The lungs were clear. The heart was not enlarged, had sounds of good muscular quality, regular sinus rhythm, and a rate varying from 90 to 120. Blood pressure 156/92. The impression was that the patient had arteriosclerotic heart disease.

The electrocardiogram showed severe myocardial changes suggestive of infarction of the posterior basal portion of the left ventricle.

The patient was treated with bed rest and digitalis. After a period of three weeks he left the hospital contrary to the advice of the staff.

The patient was readmitted to the hospital June 7, 1939. His complaints were similar to those of his first admission, namely, severe pain over the precordium and also pain in the back and marked weakness. In addition, he noted, also, swelling of his ankles.

Examination now showed an emaciated, white male, appearing chronically ill. He was extremely restless and uncooperative. There was definite dyspnea, orthopnea and moderate cyanosis. There was no enlargement of the thyroid gland, no exophthalmos and no tremor of the tongue or hands. There was, however, bilateral ankle edema. The lungs showed numerous moist râles at both bases. The heart showed very distant

sounds, had a regular rhythm and a rate of 124. Blood pressure 124/76. It was felt that the patient had a severe form of arteriosclerotic heart disease. The marked emaciation and the tachycardia suggested also the possibility of a hyperthyroidism.

The basal metabolic rate was plus 117. The blood chemistry showed a cholesterol of 148, sugar 87, nonprotein nitrogen 39, and uric acid 3 mg per 100 cc. A roentgenogram of the heart did not show any enlargement. The electrocardiogram showed a sinus tachycardia and evidence of moderate myocardial damage.

After 15 days' preparation a right hemisubtotal thyroidectomy was performed, June 28, 1939. There was a decided improvement in the clinical condition following this operation.

On July 11, 1939, a left lobe subtotal thyroidectomy was performed. His post-operative course was uneventful, and his improvement progressive. There was a complete change in the clinical picture. The patient gained weight, was cheerful and co-operative. The basal metabolic rate was now plus 12. He was discharged, August 13, 1939, in excellent condition, having gained 27 lbs.

The pathologic diagnosis of the right lobe was a hyperplastic goiter and the left lobe was that of a colloid goiter with a few intravascular papillary projections.

Comment—While it is our feeling that this patient undoubtedly had some myocardial damage suggestive of a posterior basal infarct he suffered also from a severe form of thyrotoxicosis. His failure to respond adequately to bed rest and digitalis, the emaciation and persistent tachycardia suggested a diagnosis of hyperthyroidism, which was confirmed by the unusually high basal metabolic rate. It is to be noted, also, that in this instance the cholesterol was markedly reduced. The thyrotoxicosis unquestionably increased the severity of the associated heart disease. The patient's recovery following operation was little short of astounding.

Case 7—B. S., male, age 62, when seen, April 2, 1932, complained of abdominal pain, slight diarrhea of eight months' duration. For the past month he also had precordial pain, and had lost 16 lbs. The abdominal pain which was localized in the epigastrium, would occur about one hour after eating and was relieved by food.

Physical examination revealed an elderly, undernourished apathetic patient, appearing chronically ill. There was no exophthalmos but a slight stare. The isthmus of the thyroid gland was palpable. The lungs showed moist râles at both bases. The heart was not enlarged and had a rapid irregular rhythm. There were no murmurs. There was a pulse deficit of 24. Blood pressure 110/60. The abdomen was slightly distended and showed marked tenderness in the epigastrium. The liver edge was felt two fingers' breadth below the costal margin. There was pretibial edema.

The electrocardiogram showed auricular fibrillation. A roentgenogram of the gastrointestinal tract showed a persistent deformity of the duodenal bulb, indicative of duodenal ulcer.

The patient was put on an ulcer regimen, and he improved promptly. The abdominal pain disappeared and the diarrhea stopped. He also gained several pounds in weight.

This improvement, however, was only temporary, and within two months, most, if not all, of his original symptoms returned. He developed in addition a severe cough productive of blood-streaked expectoration.

During the following two years the clinical course was progressively downward with an occasional remission in his symptoms. In view of his asthenia, weight-loss, and cough with blood-streaked sputum, it was deemed advisable to investigate the patient from the standpoint of pulmonary tuberculosis. Accordingly, he was hospitalized for a period of three weeks. The physical findings were essentially those previously recorded.

Gastro-intestinal roentgenograms showed, now, overactivity of the duodenal cap but

not a persistent defect. This suggested the possible presence of a duodenal ulcer but was not conclusive. The roentgenogram of the lungs suggested the presence of a small amount of infiltration in the right apex and of old tuberculous emphysematous bullae in both upper lobes and diaphragmatic adhesions on both sides. The sputum was negative for tubercle bacilli. Two basal metabolic rate tests showed plus 26 and plus 36, respectively.

It was thought, now, that the patient had hyperthyroidism, and that this was responsible for his symptoms of asthenia, weight-loss, epigastric pain and congestive heart failure with auricular fibrillation which failed to respond to digitalis. Following a 12-day period of preparation with Lugol's solution, there was a marked improvement in all his symptoms.

On March 3, 1934, a subtotal thyroidectomy was performed. Prompt improvement followed operation. At the time of his discharge from the hospital, March 27, he was symptom-free and showed a gain in weight of 5 lbs. His heart showed a regular sinus rhythm and a rate of 72. The basal metabolic rate was plus 8.

The pathologic diagnosis of the removed gland was colloid adenoma of the thyroid gland with several scattered areas of typical hyperplasia with intravascular papillary projections.

Comment—The patient during the different stages of his clinical course was considered to have peptic ulcer, pulmonary tuberculosis and heart disease. Not only the clinical findings but also the laboratory data supported, to a certain extent, these various diagnoses. Indeed, it required repeated roentgenographic studies to rule out the presence of duodenal ulcer and of active pulmonary tuberculosis. Persistence of his asthenia, of his epigastric pains, and the weight-loss, in addition to the auricular fibrillation and congestive heart failure, which failed to respond to digitalis, suggested, finally, the diagnosis of hyperthyroidism. This was confirmed by a moderate increase in his basal metabolic rate and a definite improvement following Lugol therapy. Operation resulted in a complete, permanent recovery, with a total disappearance of all gastro-intestinal and cardiac symptoms.

Case 8—M. C., female, age 35, seen for the first time June 22, 1939, complained of cardiac palpitation, considerable loss of weight, swelling of the feet, slight cough, occasional hemoptysis, and epistaxis of two years' duration. At one time during this period tuberculosis was suspected but was ruled out by the negative physical findings, negative sputum and negative roentgenologic studies.

Physical examination showed an emaciated young female, appearing chronically ill. There was no exophthalmos. The isthmus of the thyroid was just barely palpable but there was no discernible enlargement of either lobe. The lungs showed moist râles at both bases. The heart was not enlarged to percussion, had a regular rhythm and a rate of 120. There were no murmurs. The liver was felt two fingers'-breadth below the costal margin and was slightly tender. There was slight pretibial edema. The hands were not moist and showed a very slight tremor. Blood pressure 180/100. Fluoroscopy showed the lungs to be clear and the heart to be of normal size and shape. There was no evidence of a substernal goiter.

A diagnosis of hyperthyroidism was made and the patient was hospitalized. Following 11 days' preoperative therapy with bed rest, high calory diet and Lugol's solution a definite improvement occurred. On July 4, 1939, a subtotal thyroidectomy was performed. The postoperative course was uneventful. The patient was discharged July 12, 1939, in excellent condition.

The pathologic diagnosis of the thyroid removed at the operation was hyperplastic goiter

A follow-up examination, August 14, 1939, showed the patient to be symptom-free. Her weight was 123 lbs. The heart rate was 78 and the blood pressure 140/70. The basal metabolic rate was minus 13.

Comment—In this case the diagnosis of pulmonary tuberculosis was entertained for awhile, because of the hemoptysis and persistent weight-loss. This diagnosis, however, was definitely ruled out by sputum examination and roentgenographic study of the lungs. Subsequently, the patient presented symptoms of congestive heart failure. In the absence of pulmonary tuberculosis, the presence of tachycardia and weight-loss led to the diagnosis of hyperthyroidism. Relief resulted after a diagnosis had been established from the administration of Lugol's solution and thyroidectomy.

Case 9—Z J, female, age 65, when first seen April 1, 1932, complained of non-productive cough, dyspnea, substernal distress, cardiac palpitation and weakness of one year's duration. She had been, also, a mild diabetic of many years' standing.

Physical examination revealed a small, fairly well-nourished elderly female, weighing 126 lbs. The eyes showed no exophthalmos. The thyroid gland was neither enlarged nor palpable. The lungs were clear. The heart was not enlarged to percussion and had no murmurs. The rhythm was regular and the rate was 88. Blood pressure 140/80. Urine Specific gravity 1.020, negative for albumin and sugar. Blood sugar 100 mg per 100 cc.

She was kept under observation for a period of two years, during which time the clinical picture remained unchanged.

On May 31, 1934, she complained of progressive weakness and moderate weight-loss. Pulse 96, blood pressure 170/70. Weight 111 lbs. The urine showed 15% sugar, blood sugar 150 mg per cent. A roentgenogram of the chest showed a small substernal goiter. The basal metabolic rate was plus 66. This established the diagnosis of hyperthyroidism.

Following iodine therapy, the patient showed a gain of 3 lbs in weight, a drop of pulse rate to 78, and blood pressure 140/80, and a reduction in the basal metabolic rate to plus 38.

A subtotal thyroidectomy was performed June 13, 1934. Except for the development of auricular fibrillation which lasted eight days, her postoperative course was smooth, and her recovery was complete.

The pathologic report on the removed specimen was adenoma of the thyroid gland with moderate hyperplastic changes and vesicles filled with colloid. The diagnosis was toxic adenoma.

When followed up, July 26, 1936, the patient was in excellent condition. Her weight was 130 lbs, the heart was regular and had a rate of 78. Blood pressure 110/60, basal metabolic rate minus 10. Blood sugar 120 mg per 100 cc, and the urine was sugar-free.

Comment—This is an instance of hyperthyroidism masquerading as diabetes mellitus, associated with angina pectoris. While progressive weakness in the presence of diabetes of only moderate severity aroused some suspicion, the diagnosis of hyperthyroidism was not seriously considered until a substernal goiter was discovered roentgenologically. Thyroidectomy resulted in marked improvement in the clinical picture including the diabetic state.

Case 10—O U, female, age 66, when seen, March 9, 1940, complained of dizzy spells, weakness, cardiac palpitation and orthopnea of three years' duration. There was a

slight loss of weight These symptoms were aggravated during the past month, following an attack of gripe Her past history revealed that she had had hypertension since 1929 In 1938 she was treated for cardiac decompensation

Physical examination showed a well-developed female, moderately emaciated and dyspneic Her weight was 116 lbs There was no exophthalmos On palpation of the thyroid gland one could feel the isthmus and a small nodule of about 2 cm in diameter in each lateral lobe The heart was enlarged to the left, had an irregular rhythm and a rate of about 120 There was a pulse deficit of 22 The aortic second sound was markedly accentuated A loud systolic murmur was heard all over the precordium Blood pressure 204/120 The liver was tender and was palpable three fingers' breadth below the costal border There was no tremor

The blood cholesterol was 200 mg per cent The basal metabolic rate was plus 58 The electrocardiogram showed left axis deviation but no other striking changes The urine was essentially negative

A diagnosis of hyperthyroidism was made The patient was hospitalized, March 10, 1940, and was treated for 12 days with Lugol's solution The basal metabolic rate dropped to plus 22

On March 21, a subtotal thyroidectomy was performed Her convalescence was uneventful and her recovery complete

The pathologic diagnosis was toxic adenomata with colloid changes

A check-up on September 21, showed a regular heart rate of 80 and a blood pressure of 160/100 Weight 135 lbs Basal metabolic rate plus 6 She had, now, a glycosuria and a blood sugar of 197 mg per cent

Comment—This case represents the typical thyrocardiac in which symptoms of myocardial failure were predominant The presence of thyrotoxicosis was entertained because of the weakness, weight-loss and the rapid irregular rhythm suggestive of auricular fibrillation The symptoms were entirely relieved by a compound solution of iodine and thyroidectomy It is to be noted that the irregular rhythm which appeared to be that of auricular fibrillation cleared up following the administration of iodine Unfortunately, no electrocardiogram was made of the arrhythmia Although there was a temporary improvement in the hypertension, it did not persist This is not uncommon, as has been pointed out by Boas and Shapiro⁴ It is to be noted, also, that diabetes occurred following thyroidectomy The significance of this is difficult to determine

Case 11—G W, female, age 39, when first seen June 1, 1938, complained of thumping in the head and pain in the back of the neck, nervousness, cardiac palpitation and precordial pain of three months' duration There was also a considerable loss of weight over a period of several years, from 161 to 128 lbs

Physical examination revealed a fairly well-nourished female who did not appear chronically ill The eyes showed no exophthalmos The thyroid gland was slightly enlarged and smooth The heart was not enlarged, had a normal rhythm and a rate of 90 Blood pressure 150/90 The lungs were clear There was no tremor Basal metabolic rate plus 33

A diagnosis of hyperthyroidism was made and the patient was hospitalized, June 15, 1938 Following an eight-day period of preparation with Lugol's solution, the patient was anesthetized with avertin-cyclopropane anesthesia which resulted in an acceleration of the heart rate to 130 and an irregular rhythm The operation was, therefore, deferred Following three more days of preparation, a subtotal thyroidectomy was performed

The patient made an uneventful recovery and was discharged from the hospital, June 30 1938, at which time her heart rate was 72, and the blood pressure 120/70. She was entirely symptom-free.

Pathologic examination of the glandular tissue removed showed acini with frank hyperplastic changes. There was an unusual degree of lymphatic infiltration, both diffusely and in aggregations. The findings were those of mixed hyperplastic and colloid goiter.

A follow-up, March 8, 1939, showed the patient to be in excellent condition and entirely free from symptoms. Weight 138 lbs., heart rate around 70. Basal metabolic rate minus 5.

Comment—This case is an example of hyperthyroidism resembling a neurasthenic state. Indeed, it would have been difficult to attribute her symptoms definitely to thyrotoxicosis if it were not for the very decided improvement which followed the use of Lugol's solution, and particularly after thyroidectomy.

Case 12—M. O., male, age 55, when seen, October 19, 1940, complained of anorexia, loss of 40 lbs. in weight, and diarrhea of six weeks' duration. There were also attacks of abdominal colic, and on a few occasions episodes of vomiting. There was occasional cardiac palpitation. His previous history was entirely negative.

Examination showed a well-developed male, looking rather chronically ill. There was no exophthalmos and, indeed, the eyes seemed sunken in appearance. The thyroid gland could not be felt. The heart was not enlarged, had a regular rhythm and had a rate of 88. There was a short systolic murmur at the apex. The lungs were entirely clear. The abdomen was scaphoid and presented no masses. There was, however, some tenderness in the epigastrium. The liver and spleen were not felt. The hands showed a very fine tremor. Weight 156 lbs. Blood pressure 150/90.

The gastro-intestinal series was entirely negative. The basal metabolic rate was plus 48. A definite diagnosis of hyperthyroidism was made. The patient was then prepared for operation by administering Lugol's solution from October 29 to November 11. Following this regimen his weight increased to 165 lbs., the diarrhea stopped, and his appetite improved.

On November 13, 1940, a subtotal thyroidectomy was performed. His recovery was uneventful, and he was discharged from the hospital, November 20, 1940.

The pathologic diagnosis of the removed gland was mixed hyperplastic goiter.

Comment—This represents a case of thyrotoxicosis masked as some form of gastro-intestinal disease. No pathology in the gastro-intestinal tract was found roentgenologically. The presence of a fine tremor of the hands led us to suspect hyperthyroidism as the cause of his gastro-intestinal manifestations. Prompt and marked improvement followed the employment of Lugol's solution and thyroidectomy.

COMMENT—The term masked hyperthyroidism applied to this series of patients connotes that the evidence of thyrotoxicosis is obscured by symptoms and signs of other clinical entities. As shown in Table I, the usual obvious signs and symptoms of toxic goiter were not present at all, or only to a slight degree. For purpose of classification the cases fall into groups depending upon the clinical entities which they resemble. This grouping is shown in Table II. In most instances the patient presented more than one clinical pattern.

MASKED HYPERTHYROIDISM

Case No	Sex	Age	Exop	Goiter	Tachy	Tremor	Nervousness	Sweating	Dyspnœa	Palpable	Cong Heart Failure	Aur Fib	Precord Pain	Vomiting	Diarrhea	Ab Pain	Anorexia	Wt Loss	Weakness	Blood Pressure	Glycosuria	B M R
1	M	60	-	-	Mod	-	-	-	+	+	-	-	+	-	-	-	-	+	+	155/60	+	+50
2	F	36	-	Very sl	Marked	-	+	Sl	+	+	+	+	-	-	-	-	+	+	+	220/140	-	+82
3	F	59	-	Sl	-	-	-	-	+	+	-	-	-	+	-	+	-	+	+	200/60	-	+71
4	F	52	-	Nodule	Sl	-	-	-	+	+	-	-	-	-	-	+	-	+	+	150/80	-	+38
5	F	56	-	Nodule	-	-	+	-	+	+	-	-	-	-	-	-	-	+	+	140/70	+	+36
6	M	58	-	-	Mod	-	-	-	+	+	+	-	+	-	-	-	-	+	+	156/92	-	+117
7	M	62	Sl stare	-	+	-	-	-	+	-	+	+	+	-	-	+	-	+	+	110/60	-	+36
8	F	35	-	-	Mod	Sl	-	-	-	+	+	-	-	-	-	-	-	+	+	180/100	-	+54
9	F	65	-	-	-	-	-	-	+	+	-	-	+	-	-	-	-	+	+	140/80	+	+66
10	F	66	-	Mod	Mod	-	-	-	+	+	+	-	+	-	-	-	-	+	+	204/120	-	+58
11	F	39	-	Sl	-	-	+	-	-	+	-	-	+	-	-	-	-	+	+	150/90	-	+33
12	M	55	-	-	-	Sl	-	-	-	+	-	-	-	+	-	+	-	+	+	150/90	-	+48

TABLE I
SYMPTOMS AND SIGNS IN 12 INSTANCES OF MASKED HYPERTHYROIDISM

TABLE II
GROUPING ACCORDING TO SIMULATED ENTITIES

	Simulated Diseases	Number of Cases
I	Heart diseases	9
II	Gastro intestinal disturbance	4
III	Diabetes mellitus	3
IV	Hypertension	2
V	Neurosis	2
VI	Pulmonary tuberculosis	2

By far the largest and most important group was that in which there was present a clinical picture of some circulatory disorder, namely, congestive heart failure, auricular fibrillation, tachycardia, or angina pectoris. Nine of our patients showed symptoms and signs of circulatory disorder. The most frequent symptom was cardiac palpitation, being noted in seven instances. Definite signs of congestive heart failure were present in five of the cases. Dyspnea was the outstanding symptom in five instances. Four of the patients presented an anginal syndrome. Auricular fibrillation was noted in three instances. In one patient marked tachycardia was the outstanding symptom.

Two of the patients (Cases 3 and 7) with congestive heart failure and auricular fibrillation showed a striking degree of apathy. They were similar to the group of cases, "Apathetic Hyperthyroidism," described by Lahey.⁹ Undoubtedly, the patients with congestive heart failure, with or without auricular fibrillation, had preexisting organic heart disease, largely of the arteriosclerotic type. It is our belief, also, that the patients with angina pectoris suffered from pathologic hearts on the basis of coronary artery disease. Indeed, in one case (Case 6) with congestive heart failure and angina, definite signs of myocardial infarction were noted in the electrocardiogram. As pointed out by Hamburger and Lev,⁷ these cases might be regarded as instances of latent angina pectoris, in whom the thyrotoxicosis served to convert their latent angina to an active one because of the burden it imposes.

In four instances the patients presented symptoms referable to the gastrointestinal tract. These included anorexia, vomiting, abdominal pain and diarrhea. The additional symptoms of weight-loss and asthenia in two of the cases suggested a diagnosis of some form of gastro-intestinal malignancy. In one instance the diagnosis of peptic ulcer was entertained because of the definite time relationship of the pain to meals and relief by food. Indeed, in this case the roentgenogram showed hyperperistalsis of the duodenum but no persistent defect. It should be noted that subtotal thyroidectomy completely relieved these various complaints.

In three instances the hyperthyroidism was masked by diabetes mellitus, which was only of moderate severity and persisted even after thyroidectomy. In this connection it should be noted that there is a definite disturbance of carbohydrate metabolism in about 35 per cent of the cases of hyperthyroidism. This disturbance bears no relation to the severity of the hyperthyroidism. The storage mechanism of glycogen in the liver appears to be impaired. However, it is not the liver alone which is responsible for the carbohydrate

metabolism disturbance, for when the patient recovers from the hyperthyroidism, he still remains a diabetic

The usual form of hypertension found in hyperthyroidism is a moderate elevation of the systolic without a corresponding rise in the diastolic pressure. There are, however, instances with pronounced elevation in both systolic and diastolic pressures. In these cases an underlying hyperthyroidism may be entirely obscured by the hypertension, which, as a rule, persists even after thyroidectomy. This was observed in two of our cases (Cases 2 and 10). It is probable that these patients have an associated essential hypertension or some form of diffuse vascular disease. In this connection, it will be recalled that Boas and Shapiro⁴ regarded a group of cases of hyperthyroidism with diastolic hypertension as a special syndrome to be distinguished from the ordinary form of hypertension and from exophthalmic goiter.

Hyperthyroidism associated with symptoms of neurasthenia or symptoms suggesting pulmonary tuberculosis, was more difficult to recognize. In these instances a long period of clinical observation and careful evaluation of suggestive signs made the diagnosis possible.

While these various types of masked hyperthyroidism are the only ones that we have encountered, there are, undoubtedly, other forms which with further study will come to light. We have already referred to a group which masquerades as progressive muscular dystrophy or myasthenia gravis. As emphasized by Hamburger and Lev,⁷ these cases of masked hyperthyroidism "are important because of the difficulty of recognizing them, because of their frequency and, particularly, because of the brilliant results that are obtainable by correct diagnosis and treatment."

SUMMARY AND CONCLUSIONS

(1) We have presented a series of 12 cases of masked hyperthyroidism, dividing them into groups depending upon the clinical entities which they resemble.

(2) Great emphasis was laid on the importance of bearing in mind the possibility of thyrotoxicosis when a patient presents an atypical clinical picture of some other type of disease, particularly organic heart disease, with or without congestive heart failure, angina pectoris or auricular fibrillation, diabetes mellitus, hypertension, some form of gastro-intestinal disturbance, or a psychoneurosis.

(3) It was pointed out that the diagnosis of masked hyperthyroidism, in addition to the points mentioned, was based on certain suggestive signs and symptoms as persistent moderate tachycardia, unexplained weight-loss, an increase in the basal metabolic rate, improvement or relief of symptoms, decrease in the basal metabolic rate following iodine medication and thyroidectomy, and, finally, the histologic report of the removed gland.

(4) We have stressed the importance of recognizing this frequently misdiagnosed group of cases because of their relative frequency and particularly because of the brilliant results that follow surgical treatment.

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THE END-RESULTS OF THYROIDECTOMY

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FOREWORD

A FRANK, detailed, honestly compiled presentation of results in a fairly standardized surgical procedure is a most wholesome exercise for any surgeon, but particularly advantageous for the young surgeons in training. As stated by the authors, most of the thyroidectomies included in this series were performed by the resident surgeons, whose periods of training before their residency ranged from three to five years.

The survey, conducted carefully over a period of years, disclosed a very definite improvement in mortality and morbidity in the latter half of the series, an improvement which may well be attributed to the application of lessons learned from a critical analysis of current experiences, from which all members of the staff benefited. Such studies should be included as part of the regular training of the resident staff.

There have been relatively few reports of the end-results of thyroidectomy from nonendemic goiterous regions. We wish to present the results obtained in 341 consecutive patients operated upon for disease of the thyroid in the Clinic Service of the Stanford University Hospital. The shortest period of observation is six months, and the longest 13 years. Particular attention was paid to a study of the postoperative complications.

The types of cases encountered in this series are classified in Table I.

TABLE I

CLASSIFICATION OF TYPES OF THYROID DISEASE ANALYSED

Type	Female	Male	Total
Diffuse toxic goiter	116	41	157
Adenoma			
Nontoxic	66	12	78
Toxic	69	6	75
Colloid goiter	15		15
Chronic thyroiditis	7		7
Tuberculosis		1	1
Neoplastic			
Benign (fibroma)	1		1
Carcinoma	3	3	6
Lingual	1		1
Totals	278	63	341

Preoperative Treatment—All of the patients with hyperthyroidism, either mild or severe, were admitted to the Medical Service for preparation before surgery. Patients in whom there was no evidence of hyperthyroidism were usually admitted directly to the Surgical Service. On the Medical Service a fairly standardized treatment was instituted, the main variation being its duration before operation. Bed rest, preferably in a room apart from the ward, was imposed. A high caloric (3,500 calories daily) high vitamin diet was administered, supplemented by vitamin concentrates. Fluids were given as desired except two hours before operation when 1,000 cc of 10 per cent glucose in normal salt solution was administered intravenously. One-half grain of phenobarbital was given routinely three or four times daily. Any patients showing signs of cardiac failure were treated accordingly. Iodine (in some form) was given to all toxic patients, by far the most common preparation being Lugol's solution, ten drops three times daily. The period over which this treatment was kept up varied from ten days to one month. There was no evidence that continuation of the treatment for more than ten days to two weeks brought on "iodine escape," and in a few of the patients who did not do so well postoperatively we thought the amount of iodine inadequate. The patients who had been treated with iodine intermittently or who had had iodine continuously for a long time prior to hospital entry usually did not respond as well as those who had had no iodine, and consequently a longer period of bed rest before operation was required.

The basal metabolic rate was determined on entry before treatment was started and every few days thereafter until the operation was performed. Blood, urine, stool and Wassermann reaction were studied. A roentgenogram of the chest was made to show the size of the heart, the condition of the lungs, and the possible presence of a substernal thyroid. Electrocardiograms were taken routinely. Determinations of the blood cholesterol were made routinely at first, but recently were omitted, because the information obtained was not very helpful. Studies of the creatine and creatinine in the urine seem to be of more value. The larynx was routinely examined before operation to note the motility of the vocal cords.

The criteria of improvement and of readiness of the patient for operation were (1) The decrease or disappearance of the patient's symptoms, (2) the lowering of the pulse rate, and (3) the lowering of the basal metabolic rate. There was no limit set to which the pulse rate and basal metabolic rate must fall, but it was not until both of these had dropped to a stationary level and remained there for several days that the patient was considered ready for operation.

Operative Technique—Silk technic, without drainage, has been employed since 1925 in all operations performed under the supervision of Dr. Emile Holman. In most of the adenomata, mildly toxic or nontoxic, a subtotal thyroidectomy was performed, leaving a fairly liberal portion of the gland. Subtotal thyroidectomies, leaving only a very small portion of the gland, were undertaken in the toxic, diffuse goiters and in the severely toxic adenomata.

The majority of the thyroidectomies were performed by the resident surgeon, some of the more seriously toxic patients being operated upon by the staff. Twenty-three surgeons operated upon these patients during this period.

The technic of subtotal thyroidectomy as used in most of the cases was that taught the resident surgeon by the visiting staff, and consisted substantially as follows. The anesthesia employed in practically all cases was nitrous oxide and oxygen, preceded in recent cases by avertin. Several cases were operated upon entirely under local anesthesia supplemented occasionally by avertin.

A short, low incision was made in the folds of the skin 2-3 cm above the suprasternal notch. The incision was carried through the skin, and platysma muscle. The bleeding points were tied with fine silk. The upper flap was dissected to the lower border of the thyroid cartilage and the lower flap to the manubrium. A vertical incision was made in the middle cervical fascia down to the isthmus of trachea, the prethyroid muscle, the sternohyoid, the sternothyroid, and the omohyoid muscles were retracted laterally, the sternohyoid and sternothyroid muscles being first separated by blunt dissection. Only rarely, in very large glands, was it necessary to divide the middle cervical fascia and prethyroid muscles to obtain exposure. The thyroid was exposed by displacing the sternothyroid muscle laterally and the extracapsular areolar tissue by blunt dissection. The right superior pole of the gland was exposed, and the superior thyroid artery and vein isolated by blunt dissection and doubly clamped. The vessels were cut between the clamps and doubly ligated with double medium silk. The superior pole was retracted downward and outward, freeing it laterally and from the trachea. The middle thyroid vessels were ligated and cut. The inferior thyroid vessels were ligated close to the gland and cut. A row of hemostats was placed on the vessels on the lateral side of the right lobe, marking out the amount of gland to be left on that side following amputation of that lobe. The isthmus was divided. The right lobe was amputated from within outward leaving a small shell of gland approximately $3 \times 1 \times 0.5$ cm on the posterior capsule.

Occasionally during the past two years, the vocal cords have been examined by direct laryngoscopy after the removal of one lobe and at the conclusion of the operation. The left lobe was then excised in a manner similar to that described for the right. The wound was closed without drainage except in large substernal goiters. During the operation the patients received 1,000-1,500 cc of normal salt solution by hypodermoclysis.

Postoperative Care—The proper care of the patients following thyroidectomy was considered most important. After their return to the ward they were temporarily placed in a semi-Fowler position. Frequent change of position was stressed. For the first 24-48 hours they received 300 cc of tap water by rectum every four hours. Thirty grains of sodium bromide was usually given in the first and third rectal instillations. Lugol's solution, minimis ten, was administered three times daily by mouth or in the rectal tap.

water Morphine sulphate 0.01-0.015 Gm was administered hypodermically every four hours as needed for pain or restlessness. In the severely toxic patients oxygen was administered during the first 24-48 hours. Usually the patients began to take hot water by mouth 12 hours after operation and a liquid diet on the second day. All stitches were removed on the second postoperative day. The patients were usually up on the fifth or sixth day and left the hospital on the seventh. A postoperative laryngeal examination was always made.

The toxic cases were kept on Lugol's solution, minimis five, three times daily for four months postoperatively to prevent too rapid regeneration of the remaining thyroid. The patients were followed in the Thyroid Clinic every month for three months, then every two months for one year and then every six months thereafter. Check-up determinations of basal metabolisms were made one month postoperatively and when indicated thereafter.

POSTOPERATIVE COMPLICATIONS

TABLE II

SUMMARY OF POSTOPERATIVE COMPLICATIONS

(1) Wound	17
(a) Infections	2
(b) Hematomata	6
(c) Serum	9
(2) Tetany	8
(3) Pulmonary	6
(4) Toxic psychoses	2
(5) Thyroid crises	6
(6) Burns (prep sol.)	2
(7) Recurrences (1 goiter only)	10
(8) Vocal cord palsies	31
(9) Deaths	5

(1) *Wound Complications*—There were 17 wound complications. These varied from small serum collections to infections.

(a) Two wounds were infected, one in which catgut technic was utilized and the wound drained, and the other in a patient closed with silk.

(b) Hematomata developed in six cases. The hematomata were aspirated or evacuated, and the time of wound healing was not prolonged in most cases. Postoperative hemorrhage, in two cases, was sufficiently severe to require the return of the patients to the operating room for religation of bleeding points.

(c) In nine cases, all closed with catgut, there were serum collections requiring aspiration or drainage.

(2) *Tetany*—Eight patients had tetany postoperatively. Six of the cases were mild and required small amounts of calcium by mouth for from one to three weeks. One of the cases of tetany was moderately severe, requiring calcium and parathormone. She had a positive Chvostek for six months. One patient had severe postoperative tetany. Her blood calcium fell to 6.2 mg per cent, and the blood phosphorus rose to 5 mg per cent. She re-

quired parathormone and intravenous calcium chloride. Later, it was possible to control the tetany with viosterol and calcium by mouth. Two years after the thyroidectomy she still needs four drops of viosterol and two table-spoonfuls of calcium daily.

(3) *Pulmonary Complications*—Six patients had postoperative pulmonary complications. Two patients had atelectasis. In both cases the atelectasis occurred on the second postoperative day and entirely cleared up in two days. Four patients had bronchopneumonia. One of these patients died two days after operation.

(4) *Toxic Psychoses*—Two patients exhibited toxic psychoses after operation. Neither had had mental symptoms prior to operation. Both developed delusions of persecution which entirely cleared up within three weeks after the operation.

(5) *Thyroid Crises*—Six patients ran stormy postoperative courses, characterized by fever, rapid pulse and rapid respiration. One of the patients was operated upon in two stages, the first being a lobectomy and polar ligation. She ran a stormy course after each stage. Each of these patients had high basal rates, and two of them had had previous attacks of auricular fibrillation.

(6) *Burns*—Two patients received mild burns upon the upper back from puddling of the solutions used for skin preparation. Solutions used in these cases were ether, alcohol and 4 per cent tincture of iodine.

(7) *Recurrences*—Nine patients in this series had a recurrence of their toxic symptoms. One patient, operated upon for a nontoxic adenoma, later developed another adenoma. Five of the patients with recurrent toxic symptoms were reoperated upon with complete relief of symptoms. The patient with a recurrence of nontoxic adenoma declined another operation. Three patients with mild toxic symptoms were treated with roentgenotherapy with complete relief of symptoms. One patient, who is mildly toxic, is being carried along on small doses of iodine.

(8) *Vocal Cord Palsies*—Routine postoperative examination of the vocal cords showed a paralysis of one cord in 30 cases and a temporary paralysis of both cords in one case. No patients have lost their voices nor have they had respiratory difficulties. The patient with the temporary bilateral cord palsy had tuberculosis of the thyroid. It was considered to be carcinoma at the operation, and a radical excision was performed. The function of both cords returned in six months. In at least seven of the unilateral cord palsies the function of the cord returned after four to six months.

In two of the cases thyroidectomy was performed for carcinoma and the recurrent laryngeal nerve was deliberately sacrificed on one side. Five of the palsies occurred in cases of recurrent goiter and the operation was more difficult because of the scarring.

(9) *Fatalities*—Five patients died during or after operation, mortality rate for all cases of 1.46 per cent. Three of the deaths occurred in patients with hyperplastic toxic goiter and two in patients with toxic adenomata.

For detailed analysis of the postoperative deaths, see the summaries at the conclusion of the paper. In the period between 1932-1939, there were 192 consecutive thyroidectomies without a death.

End-Results—Tables III and IV summarize the end-results of all cases followed in this series.

TABLE III
END RESULTS OF THYROIDECTOMY DURING A 13 YEAR PERIOD

	Sex	A*	A Hypo*	B*	R*	Deaths		No F U*	Total
						H*	O*		
Diffuse toxic goiter	{ F	73	18	9	7	2	1	6	116
	{ M	28	5		1	1	2	4	41
Adenoma	{ F	49	4	5				8	66
Nontoxic	{ M	8			1†		1	2	12
Toxic	{ F	41	9	3	1	1	1	13	69
	{ M	4				1		1	6
Colloid	F	6	3	1				5	15
Chronic thyroid	F	4	2	1					7
Tuberculosis	M		1						1
Neoplastic									
Benign	F	1							1
Carcinoma	{ F						3		3
	{ M						3		3
Lingual thyroid	F		1						1
Totals		214	43	19	10	5	11	39	341

* Key (A)—Improved In good health and able to do usual work

(A Hypo)—Improved In good health but taking thyroid extract

(B)—Slightly improved No recurrence of hyperthyroidism but still complaining of symptoms noted before operation

(R)—Recurrence or continuation of hyperthyroidism

Deaths—(H)—In hospital

(O)—Sometime after leaving hospital of conditions other than those due to hyperthyroidism

No (F-U)—No follow up Patients not traced or for less than six months

†—Goiter only

TABLE IV

Total cases	341
Total cases followed	302
Total toxic cases	232
Recurrences	9
Recurrence rate	3.88%
Total operative mortality	1.46%
Complete relief of symptoms	85%
Partial relief of symptoms	6%
Total cases improved	91%

CONCLUSIONS

(1) Of 341 patients operated upon for goiter during a 13-year period, 257 are known to be improved and in good health. Nineteen are improved but still having symptoms, without hyperthyroidism. Thirty-nine patients could not be followed for a sufficient length of time to be of value in a statistical study.

(2) There were nine recurrences in 232 patients with hyperthyroidism, a recurrence rate of 3.88 per cent. The operative mortality for the entire

group was 1.46 per cent. The operative mortality in the toxic cases was 2.11 per cent.

(3) The most satisfactory results were obtained in those patients in whom a temporary hypothyroidism was obtained. A hypothyroid state is definitely desirable in patients with coronary heart disease.

(4) Paralysis of the recurrent laryngeal nerve can only be determined by routine postoperative laryngeal examinations. A clear voice is no true indication of the normal function of vocal cords. The incidence of paralysis of one cord in this series is high, as disclosed by routine laryngeal examination. Only a few were temporarily inconvenienced by hoarseness and none permanently.

(5) The postoperative administration of iodine is important in preventing excessive thyroid regeneration and recurrence of toxic symptoms.

(6) The operative treatment of hyperthyroidism continues to be the method of choice because of the rapidity with which the results are accomplished, the low operative mortality, and the low incidence of recurrence.

IODINE METABOLISM IN THYROID DISEASE

CLINICAL AND EXPERIMENTAL OBSERVATIONS

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THE SURGICAL MANAGEMENT of classic cases of hyperthyroidism has given satisfactory end-results during the past two decades. Hyperthyroidism, nevertheless, has often been confused with hypermetabolism. Not infrequently, patients are seen manifesting none of the cardinal signs and symptoms of hyperthyroidism, but in whom an elevated basal metabolic rate has been uncovered. A diagnosis of hyperthyroidism is erroneously made and surgery advised. The end-results from surgical management of this type of case have been unsatisfactory.

In contrast to patients who manifest hypermetabolism alone, are others who present symptoms suggestive of hyperthyroidism, although these may be difficult to evaluate, and in whom the basal metabolic rate is moderately elevated, usually to the extent of 15 to 30 per cent above the average normal. These patients are generally labeled "borderline" hyperthyroidism. From our experience during the past few years, an accurate diagnosis in 20 per cent of these patients has been impossible, although extensive laboratory tests including blood iodine, plasma cholesterol and galactose tolerance tests were carried out for assistance.

In this presentation, our clinical impressions on the value of blood iodine determinations in thyroid disease will be discussed. Experimental studies on the blood and thyroid gland iodine of guinea-pigs receiving equivalent amounts of iodine in various inorganic and organic combinations and thyrotropic factor of the anterior pituitary will also be summarized.

Iodine plays a significant rôle in all forms of thyroid disease. For this reason, some of the recent findings in iodine metabolism for the body at large, as well as for the thyroid gland, will be reviewed.

The human body as a whole contains approximately 40 mg of iodine distributed as follows: Muscles, 50 per cent, thyroid gland, 20 per cent, skin, 10 per cent, skeletal system, 7 per cent, and the remaining 13 per cent in other endocrine glands, organs and central nervous system (Sturm and Buchholz¹).

The thyroid gland is principally concerned with the metabolism of iodine, and this is apparent when one considers that a gland which weighs only 20 Gm contains one-fifth of all the iodine in the body. The adult human contains less iodine than that present in 7 M of Lugol's solution, since 1 M of this solution contains 6 mg of iodine (Means²). The amount of iodine necessary to keep a normal person in balance is between 100 and 200 micrograms in 24 hours (a microgram is one-thousandth part of a milligram). In

other words, one drop of Lugol's solution every 30 days is sufficient for normal iodine balance. According to Salter,³ the entire blood of a normal human contains only one-half milligram of thyroxine.

The normal physiology of the thyroid gland is a delicately balanced mechanism. The cells of the acini have apparently a dual capacity in a normal state of health. They secrete iodine into the colloid of the acini where it is stored as thyroglobulin and later the iodine is removed from the colloid and discharged into the blood stream by the same cells (Carlson and Woelfel⁴). The recent work on radioactive iodine by Hamilton, Soley and Eichorn,⁵ demonstrates that the colloid in the acini of a normal gland has the iodine evenly distributed throughout, whereas the colloid of the hyperplastic gland, without previous iodine medication, will show very little if any iodine. They show, further, that in colloid goiters, the greatest concentration of iodine is in the acinal cells and in the colloid at the periphery of the distended acini, the central portions of the colloid have little demonstrable iodine. In a normal acinus the colloid is alkaline in reaction, whereas in a long-standing distended acinus, the central portion of the colloid becomes acid and under these latter circumstances the colloid is not reabsorbable or utilizable by the cells for normal distribution (Hewer⁶). This does not prove that the distended acini of a colloid goiter contain a physiologically inactive product. By means of rapid freezing, Tatum,⁷ and van Dyke⁸ were able to separate the colloid from the cell mass, and demonstrated that 85 per cent of the iodine in the thyroid gland was in the colloid. Using the method of Tatum and van Dyke, Williamson, Pease and Cunningham⁹ isolated two types of colloid from the same gland. From that portion of the gland called inactive by histologic study, the colloid contained not only an abundance of iodine but was physiologically active by the tadpole test. The colloid from the active portion of the gland contained very little iodine and was physiologically inactive.

Maine and Lenhart¹⁰ emphasized the part played by iodine deficiency in the production of colloid goiter. They believed that first, hyperplasia of the acinal cells occurred, and that this was followed by dilatation of the acini, with atrophy and exhaustion of the cells. Maine and Lenhart found the normal thyroid gland, expressed in dry weight, contained from 0.1 per cent to 0.55 per cent iodine. Values less than 0.10 per cent represented iodine deficiency. In the New York City area, Gutman, Benedict, Baxter and Palmer¹¹ found the normal thyroid gland contained on the average 0.186 per cent iodine. In the same locality, our¹² values averaged 0.130 per cent iodine.

It is important to consider the chemical nature of iodine as it exists in the thyroid gland. Salter¹³ found that not more than 10 per cent of the total iodine in the thyroid gland was inorganic in nature, 90 per cent or more was in organic combination approximately two-thirds of which was in the form of diiodotyrosine and one-third thyroxine. In 1927, Harington and Barger¹⁴ showed that thyroxine was a derivative of tyrosine. Obviously, the first requirement necessary for the production of adequate quantities of thyroid hormone is a complete hydrolysis of ingested protein into amino-acids. Suf-

ficient amounts of tyrosine thus released must then be supplied to the thyroid gland for combination with iodine. Three iodo-amino-acids are recognized—monoiodotyrosine containing 39.1 per cent iodine, diiodotyrosine with 58.7 per cent iodine, and thyroxine containing 65.4 per cent iodine. Unlike thyroxine, the first two of these are physiologically inactive. Means, Leiman and Salter¹⁵ demonstrated a synergistic action between thyroxine and diiodotyrosine since thyroglobulin which contains both of these iodo-amino-acids was more active in the treatment of myxedema than an equivalent amount of thyroxine given alone. Abelin¹⁶ prepared a physiologically active product from the alkaline hydrolysis of iodinated casein, the administration of this material to patients with myxedema relieved their symptoms. Ludwig and Mutzenbecher¹⁷ isolated diiodotyrosine and thyroxine from iodinated casein in the same ratio as they exist in the thyroid gland. Salter and Leiman¹⁸ were able to iodinate serum albumin, and thus prepare a physiologically active substance without hydrolysis, which was also effective in relieving myxedema. These significant findings indicate that the thyroid gland may play a very small part in the manufacture of physiologically active iodine compounds as they exist in the human body.

This brings us to a consideration of disorders of the thyroid gland in localities where iodine deficiency does not exist. Can thyroid disease under these circumstances be considered as due to the lack of iodine in the body or perhaps due to a deficiency of tyrosine which supplies the organic radical? Protein metabolism, with failure to supply adequate amounts of tyrosine to the thyroid gland, may be a potent factor in the production of thyroid disease. Morton, Weeks, and one of us¹⁹ have shown that colloid goiters can be produced in dogs by the ligation of the pancreatic ducts. Under these conditions, interference with tryptic digestion might result in the incomplete hydrolysis of ingested protein with consequent failure to supply adequate quantities of tyrosine to the thyroid gland.

Experimental Studies—It is generally known that the colloid type of goiter does not respond satisfactorily to treatment with inorganic iodine. For this reason, primarily, the following experiments were carried out. Potassium iodide, sodium iodide, diiodotyrosine, thyroglobulin and thyroxine were administered to guinea-pigs in doses of one microgram of iodine per gram of body weight, every 72 hours for three doses. The animals were autopsied 72 hours after the last dose of iodine. Thyrotropic factor of the anterior pituitary⁺ (which contains no iodine) in doses of 1 cc every 72 hours, for three doses, was also given to another group of guinea-pigs. All injections were intraperitoneal. Seven to 8 cc of blood were removed from the heart just before the animals were sacrificed and the total blood iodine determined. The right lobe of the thyroid gland was analyzed for iodine content and the left lobe taken for histologic study. The iodine findings in both blood and thyroid glands are summarized in Table I.

* This material was supplied through the courtesy of Ayerst, McKenna and Harrison of Montreal, Canada, and Rouses Point, New York.

TABLE I

THE EFFECT OF THE INJECTION OF EQUIVALENT AMOUNTS OF IODINE IN INORGANIC AND ORGANIC COMBINATION AND OF THYROTROPIC FACTOR OF THE ANTERIOR PITUITARY ON THE IODINE CONTENT OF THE THYROID GLAND AND BLOOD OF GUINEA-PIGS

Group	Thyroid Gland			Whole Blood		
	No of Animals	Mean Iodine Content*	Standard Deviation	No of Animals	Mean Iodine Content γ /100 cc	Standard Deviation
Control	11	5.25	1.36	5	7.3	1.63
Potassium iodide	15	8.29	3.15	12	16.0	3.23
Sodium iodide	11	6.59	2.35	6	12.0	3.59
Thyroxine	14	5.15	1.72	12	20.9	3.36
Diiodotyrosine	12	7.71	1.94	9	9.1	3.25
Thyroglobulin	8	6.70	1.27	8	20.7	8.05
Thyrotropic factor of anterior pituitary	13	4.45	1.42	11	7.2	2.93

* These values represent the micrograms of iodine in the thyroid gland per 100 grams of body weight calculated from the following formula

$$\gamma \text{ thyroid iodine/100 Gm, body weight} = \frac{\text{Iodine content of right lobe (microgm)} \times 2 \times 100}{\text{Body weight (grams)}}$$

In 11 guinea-pigs used as controls, the mean iodine content of the thyroid gland expressed as micrograms per 100 grams of body weight was 5.25 ± 1.36 . In five of these, the mean whole blood iodine was 7.3 ± 1.63 micrograms per 100 cc. The administration of iodine in organic or inorganic combinations, as would be expected, elevated the mean thyroid and blood iodine. Although equivalent amounts of iodine were used throughout, Table I shows that diiodotyrosine and thyroxine resulted in a higher average blood iodine than that produced by iodine in inorganic combination, the increase in the iodine contents of the thyroid glands following organic or inorganic iodine were not dissimilar. The administration of thyrotropic factor of the anterior pituitary was followed by a decrease in the iodine content of the thyroid gland as has been shown previously by Closs, Loeb and MacKay,²⁰ and others^{21, 22}. The increase in blood iodine following the injection of thyrotropic factor in guinea-pigs reported by Closs and his coworkers was not observed in our animals but this may have been due to the smaller dose of hormone used in the present experiments.

Histologic studies revealed that potassium iodide, sodium iodide and diiodotyrosine in the doses administered failed to produce any noteworthy changes in the thyroid glands of the guinea-pigs. The animals receiving thyroxine and thyroglobulin gave evidence of increased cellular activity perhaps a shade more so in those injected with thyroglobulin. The guinea-pigs receiving thyrotropic factor of the anterior pituitary showed by far the greatest degree of cellular activity as indicated by hypertrophy and hyperplasia of the acinar cells. Figures 1, 2 and 3 are photomicrographs of sections of the thyroid gland of a control guinea-pig, of one injected with thyroglobulin and one receiving thyrotropic hormone, respectively, which illustrate the differences noted above.

Since Williamson, Pearse and Cunningham⁹ have shown that the so-called

"inactive" colloid is both physiologically active by the tadpole test, and contains appreciable quantities of iodine, it appears that the ideal medication for colloid goiter would be the administration of thyrotropic hormone since the resultant stimulation of cellular activity would favor resorption of the colloid by the acinar cells and reduction of the iodine content of the thyroid gland

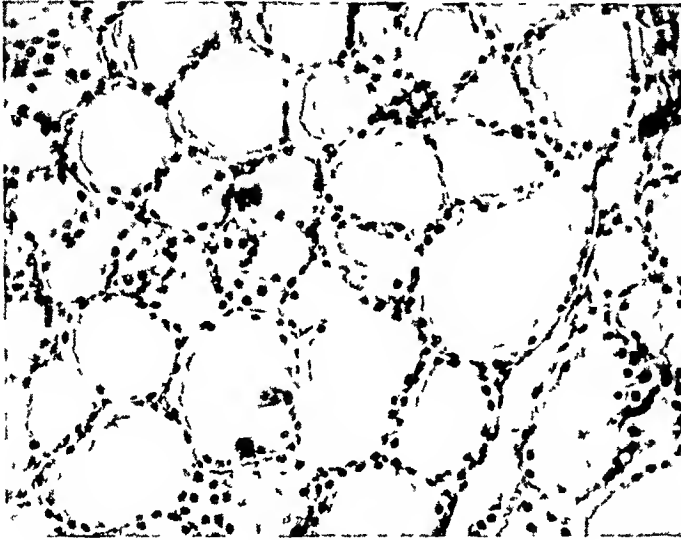


FIG 1—Photomicrograph of a section of a thyroid gland of a control guinea pig (×375)

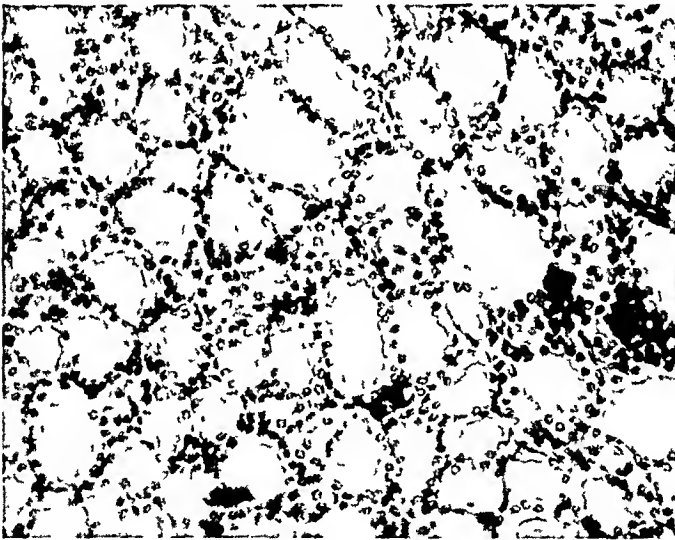


FIG 2—Photomicrograph of a section of a thyroid gland of a guinea pig receiving thyroglobulin (×375)

Theoretically, thyroglobulin and thyroxine would be less preferable, since cellular activity is not profoundly influenced as by thyrotropic hormone and, moreover, the iodine content of the thyroid gland would increase. Thyrotropic factor of the anterior pituitary is now being used for the treatment of colloid goiter in our clinic, as yet, our clinical trials have not been extensive or prolonged enough to report on its efficacy.

Studies on Blood Iodine in Thyroid Disease—Up to the present time, 303 determinations on the total iodine content of the blood have been carried

out on 236 patients, who had, or were suspected of having thyroid disease. As far as could be determined, none of the patients had been taking iodine-containing compounds within one month of the blood studies. The findings are summarized in Table II.

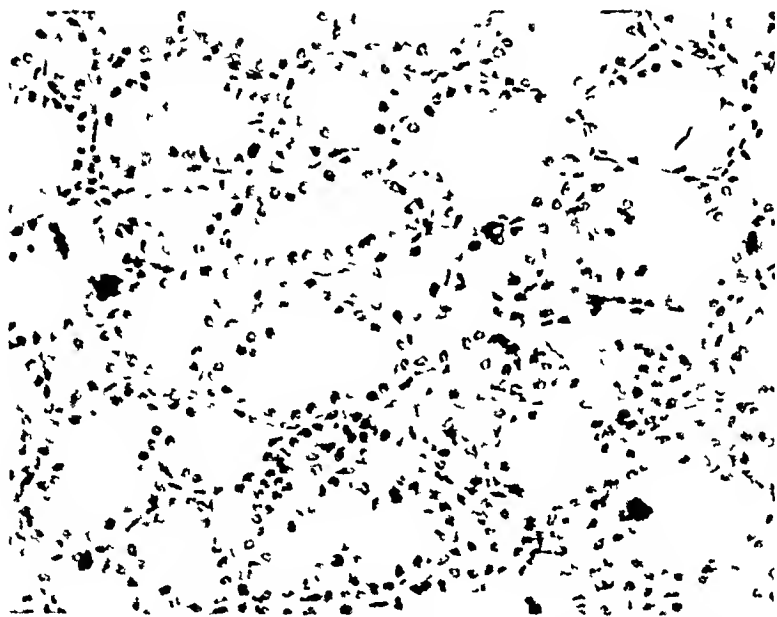


FIG. 3.—Photomicrograph of a section of a thyroid gland of a guinea pig receiving thyrotropic factor of the anterior pituitary (x 375).

TABLE II
CORRELATION OF BLOOD IODINE WITH TYPE OF THYROID DISEASE
303 Blood Iodine Determinations in 236 Patients
Whole Blood Iodine (γ per 100 cc.)

Diagnosis	No of Cases	2 to 3		3 to 9 (normal range)		9 to 30		Over 30	
		Num-ber	Per Cent	Num-ber	Per Cent	Num-ber	Per Cent	Num-ber	Per Cent
No thyroid disease	65	1	1.5	46	70.8	18	27.7	0	0
Exophthalmic goiter	66	0	0	14	21.2	50	75.8	2	3.0
Persistent exophthalmic goiter	8	0	0	6	75.0	2	25.0	0	0
Recurrent exophthalmic goiter	8	0	0	5	62.5	3	37.5	0	0
'Borderline' hyperthyroidism	8	0	0	4	50.0	4	50.0	0	0
Nontoxic nodular goiter	39	1	2.6	30	76.9	8	20.5	0	0
Toxic nodular goiter	19	0	0	10	52.6	9	47.4	0	0
Colloid goiter	11	0	0	10	90.9	1	9.1	0	0
Hypothyroidism or myxedema	12	2	16.7	10	83.3	0	0	0	0

We²³ have shown that in normal subjects, carefully selected so as to exclude, as far as possible, obvious exposure to iodine the total blood iodine varied between 3.1 and 8.4 micrograms per 100 cc. with a mean of 5.9 ± 1.3 . In 65 patients, in whom the presence of thyroid disease was eliminated (these include patients with anxiety neuroses, vasomotor instability, etc.) 18, or 27.7 per cent, had elevated blood iodine (between 9 and 30 micrograms per 100 cc.) The remainder, with one exception, showed normal values. Experience in blood iodine studies during the past three and one-half years, had taught us that such high values in patients with nonthyroid disease represent

undue exposure to iodine. It must not be overlooked that many drugs, particularly bromides, are contaminated with iodine, moreover, iodine is commonly used in many households for skin antisepsis. The use of iodine compounds in radiographic work is universal and a frequent unsuspected source of excessive iodine intake.²⁴ The fact that approximately 25 per cent of patients with nonthyroid disease show an increased concentration of total iodine in the blood does not nullify the value of such determinations in patients with thyroid disease. It merely serves to emphasize that caution should be exercised in interpreting the results of total blood iodine. Limiting blood iodine studies to the organic fraction (presumably, the circulating thyroid hormone) will probably prove to be the preferable determination. Observations on the organic iodine fraction of the blood in patients with thyroid disorders are now being carried out in this clinic, the results of which will be the subject of a later communication.

In 66 patients with exophthalmic goiter, 52, or 78.8 per cent, had an elevated blood iodine. In 32 of these, the duration of the disease was one year or less and 27, or 84.4 per cent, had an elevated blood iodine. In 34 patients, the duration of the exophthalmic goiter was more than one year, and in this group 26, or 76.5 per cent, showed an increased blood iodine. These findings are at variance with those of Perkin and Cattell,²⁵ who maintained that in long-standing cases of exophthalmic goiter, the blood iodine falls within normal limits.

The incidence of an increased blood iodine in toxic nodular goiter and in the so-called "borderline" exophthalmic goiter was approximately the same, *i.e.*, about 50 per cent. In 11 patients with colloid goiter, ten, or 90.9 per cent, showed a normal blood iodine. In 12 patients with hypothyroidism or myxedema, the blood iodine was normal in ten, or 83.3 per cent, and definitely below the normal range in two, or 16.7 per cent.

In 16 patients with persistent or recurrent exophthalmic goiter, the incidence of an elevated blood iodine was no greater than that observed in nonthyroid patients, a fact which strongly suggests that the diagnosis of hyperthyroidism, which led to surgery in these patients, may have been erroneous and that the decreased iodine content of the blood is not indicative of exhaustion of the thyroid gland. Our clinical experience alone, without the aid of blood iodine determinations, has helped to formulate this opinion.

CONCLUSIONS

(1) Subtotal thyroidectomy in patients with classic hyperthyroidism has given satisfactory end-results for the past two decades.

(2) The advent of the routine use of basal metabolic studies in patients suspected of thyroid disease has led to the confusion between hypermetabolism and hyperthyroidism. In patients manifesting an increased basal metabolism but without clinical signs of hyperthyroidism, subtotal thyroidectomy has been followed by poor end-results.

(3) The blood iodine, thyroid gland iodine, and histology of the thyroid

gland were studied in guinea-pigs following the administration of equivalent amounts of iodine in the form of potassium iodide, sodium iodide, diiodotyrosine, thyroglobulin and thyroxine. Potassium iodide, sodium iodide and diiodotyrosine elevated both the blood and thyroid gland iodine without altering the histologic picture of the thyroid gland. Thyroglobulin and thyroxine also increased the blood and thyroid gland iodine but this was associated with evidence of increased activity of the acinar cells.

(4) The administration of thyrotropic factor of the anterior pituitary (which contained no iodine) to guinea-pigs, resulted in a decrease in the thyroid gland iodine without any changes in the blood iodine. Marked stimulation of cellular activity, and diminution of the colloid content of the acini were observed following the injection of thyrotropic hormone.

(5) Approximately 25 per cent of all patients with nonthyroid disorders, though clinically suspected of having thyroid disease, had an elevated blood iodine. It is believed that a high blood iodine in such patients represents unsuspected exposure to iodine.

(6) Approximately 80 per cent of patients with exophthalmic goiter and 50 per cent with toxic nodular goiter showed an elevated blood iodine.

(7) Contrary to findings of other observers, the level of blood iodine in patients with exophthalmic goiter bore no relation to the duration of the disease.

(8) In persistent or recurrent exophthalmic goiter, the incidence of an elevated blood iodine was no greater than in patients with nonthyroid disease. Clinical experience, in addition to blood iodine studies, has helped to formulate the opinion that in many patients with persistent or recurrent exophthalmic goiter, the diagnosis of hyperthyroidism, which led to surgery, was probably erroneous and that the decreased iodine content of the blood was not indicative of the exhaustion of the thyroid gland.

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CARDIOSPASM

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CARDIOSPASM is the designation most commonly applied to a condition which other authors have called diffuse dilatation of the esophagus, idiopathic dilatation, mega-esophagus, achalasia of the cardia, or phienospasm. These numerous designations suggest that the etiology and pathology are not clearly understood. The name cardiospasm implies that we are dealing with a true spasm at the cardia. Diffuse dilatation stresses the enlargement of the organ. Idiopathic dilatation calls attention to the dilated, relaxed condition of the walls of the esophagus of unknown etiology as the outstanding condition. Mega-esophagus simply means a large esophagus, while achalasia implies the inability of the cardia to open normally. Phienospasm or phieno-esophagospasm emphasizes the pinch-cock action of the diaphragm as an etiologic factor.

Plummer¹ feels that the adoption of the term "cardiospasm" is premature and confusing, as the part that spasm of the cardia plays in the production of diffuse dilatation is by no means established. Moreover, there are many cases, probably not directly related, that have spasm at the cardiac orifice without dilatation of the esophagus.

Whatever designation is used, the diagnosis of the condition under consideration rests on finding a diffuse dilatation of the esophagus with obstruction at its lower end during the life of the patient, but without anatomic stenosis demonstrable either at operation or at postmortem examination. All other lesions have to be excluded from the discussion.

Cardiospasm is second in frequency to carcinoma in producing symptoms of esophageal obstruction. It may affect people of all ages, including infants and children. The outstanding symptoms are pain, dysphagia and regurgitation. The onset may be sudden and intermittent at first but is usually gradual with dysphagia as the only symptom. In other cases pain predominates. Later there is regurgitation of food, a sense of fullness or pressure associated with substernal or epigastric pain and possibly anemia and loss of weight. The pain may be increased by taking food or it may be independent of deglutition. Often it is very severe and radiates to the back. As the esophagus becomes more and more dilated, shortness of breath develops on exertion or on lying down. The patient may have difficulty resting at night owing to the pressure of the overloaded esophagus and because the liquid contents leak out and spill into the larynx, bringing on paroxysms of coughing. Aspiration may result and lead to pulmonary suppuration. Frequently there is loss of weight, which may assume alarming proportions.

Physical examination is negative, except perhaps for loss of weight and possible pulmonary complications. The patients may be rather nervous and apprehensive and they frequently are of the opinion that excitement, worry or fatigue are responsible for the aggravation of symptoms. Plummer¹ and Vinson,² however, who have had extensive experience with this condition, state

positively that it is not a neurosis. It is possible that the psychogenic factors are secondary to the underlying condition.

Roentgenologic examination with a contrast medium shows dilatation of the esophagus ending usually at the level of the diaphragm but sometimes at a



FIG 1—(A) Straight shadow of enormously distended esophagus. Condition present since childhood.

somewhat higher level, in a smooth, tapering constriction. This constant observation has given rise to the belief that there is a sphincter in the wall of the esophagus beginning at about the level of the diaphragm or that the diaphragm or its crura act as a pinch-cock at this point. Only very rarely has the esophageal dilatation been observed to extend to the anatomic cardia. Peristaltic waves are often observed on fluoroscopic observation and occasionally reverse peristalsis is present.



FIG 1—(B) Appearance after partial evacuation of retained contents, consisting of a frothy food mixture.

In patients in whom the condition has existed for a long time, preliminary roentgenogram of the chest may show the straight border of a shadow of increased density extending into the lung field to the right of the cardiac and upper mediastinal shadows. If this examination is made in the erect position a fluid

level may be present in the superior mediastinum due to an and retained matter in the dilated esophagus (Fig 1A) When barium is given to such a patient it is seen to float down in streams through the retained material Only very little barium enters the stomach (Fig 1B)

In some cases of long standing cardiospasm the esophagus becomes elongated and sacculated, producing an appearance simulating a diverticulum

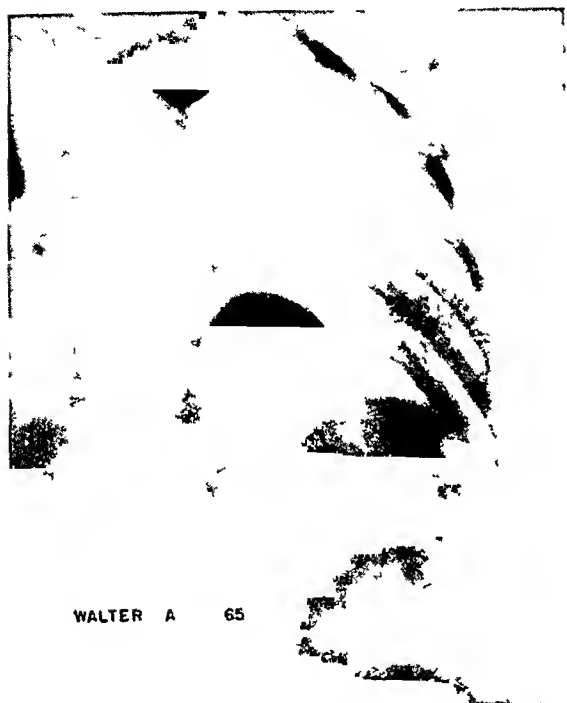


FIG 2—Enormous dilatation of esophagus with elongation and sacculation Peristaltic waves are still present



FIG 3—Cardiospasm with secondary development of diverticula

Twenty-four-hour retention in the esophagus is not uncommon (Fig 2) Actual diverticula may also develop as the result of pressure within the esophagus, causing bulging at weak portions of the wall (Fig 3)

Esophagoscopy is of great value in differential diagnosis and should be carried out whenever there is any question as to the cause of obstruction The walls of the esophagus usually look pale and flabby In older cases, with retention, the esophagus is found to be filled with frothy liquid content which has to be evacuated before visualization is possible In such cases the mucosa is congested and frequently ulcerated and the cardia may be difficult to locate The passage of an esophageal sound over a previously swallowed silk thread may be more important in diagnosis than an esophagoscopy It passes into the stomach with no more than the usual slight elastic resistance, whereas in patients with benign stenosis or carcinoma, a definite stricture can be detected

One of the very interesting observations in connection with cardiospasm is that although marked obstruction exists, which eventually leads to enormous dilatation of the esophagus, no gross anatomic change is observed or can be demonstrated below the dilatation either during operation or at autopsy

Many suggestions have been made to explain the obstruction One of the oldest is that we are dealing with a sphincter spasm This naturally presup-

poses the presence of a sphincter. However, neither at operation or autopsy has such an anatomic sphincter been demonstrated. No thickening similar to the tumor found in hypertrophic pyloric stenosis has been visualized. Knight,³ however, has recently submitted experimental evidence supporting the theory of spasm as the cause of obstruction. He has demonstrated in cats that the interdiaphragmatic and intra-abdominal portions of the esophagus function as a true intrinsic sphincter, which is relaxed by the vagus nerve and contracts on sympathetic stimulation. The sphincter is capable of functioning independently of surrounding structures and receives its sympathetic supply from the celiac plexus in fibers which follow the course of the left gastric artery and its esophageal branch to the lower end of the esophagus. He was able to show definitely with illustrations, that bilateral vagus section in cats reproduced the roentgenographic, pathologic and clinical picture of achalasia of the cardia. The sphincter failed to relax. If, however, celiac sympathectomy, with a consequent denervation of the sympathetic fibers, was performed at the same time that the vagi were divided, no obstruction resulted at the cardia, the sphincter always relaxed to allow the meal to enter the stomach. He comes to the conclusion that whether the obstruction is caused by failure of the vagus to open the cardia, or by spasm, in either case the integrity of the sympathetic supply is necessary for the obstruction to occur, and, therefore, it can be relieved by sympathectomy. In a recent anatomic study based upon careful dissection of 14 cadavers, Mitchell⁴ states that any peripheral operation to produce complete sympathetic denervation of the cardiac orifice of the esophagus would have to be more radical than the one proposed by Knight. The magnitude of an operation to interrupt all possible sympathetic fibers to the lower esophagus might be greater than is justified by the symptoms usually produced by cardiospasm.

In contrast to the theory of spasm of a sphincter at the lower end of the esophagus producing the symptoms of so called cardiospasm, Jackson⁵ believes cardiospasm is an erroneous term. He states spasm in these patients is never greater than minimal normal. He holds muscular and tendinous prolongations of the crura, which surround the esophagus, to be responsible for normal closure and opening of the lower end of the esophagus. He calls this the diaphragmatic pinch-cock. According to his theory, it is the failure of this pinch-cock to open in the deglutitory cycle, and not any excessive spasm, that is the chief etiologic factor in many cases of cardiospasm.

That the diaphragm may play a rôle in the function of the esophagus has been suggested by numerous roentgenologists who have observed temporary stoppage of the barium meal at the cardia during deep inspiration. Barsony and Wald⁶ examined their patients in a straight lateral position. In some cases of cardiospasm the barium remains arrested at the diaphragmatic hiatus during entire inspiration, even if prolonged. In other cases of cardiospasm some barium enters the abdominal part of the esophagus during the latter part of inspiration and fills the esophagus to the anatomic cardia. Therefore, in some cases, with roentgenograms taken in inspiration, the site of arrest of the barium is the hiatus, in others the cardia. The differentiation of cardia and

hiatus-spasm can often be made only if several films are taken in expiration on various phases of inspiration in straight lateral position. Mosher⁷ has made similar observations and ascribes an important rôle to the liver tunnel through which the lower part of the esophagus passes. Hurst⁸ also believes that the inability of the cardia to open, which is normally the last stage of the act of deglutition, is responsible for the dysphagia and the secondary dilatation and hypertrophy. He has applied the name "achalasia," which means inability to open, to this dysfunction, and attributes it to pathologic changes in Auerbach's plexus. This plexus is composed of ganglion cells and nerve fibers derived from the vagi, and is situated between the circular and longitudinal muscle coats. At first there is round celled infiltration, which is later replaced by fibrous tissue with complete disappearance of the ganglion cells at the lower end of the esophagus. He states that the primary cause of the change in Auerbach's plexus is unknown, but as the vagi contain the fibers which cause the sphincter to open, their degeneration results in achalasia. Rake⁹ has presented histologic evidence of the progressive degeneration of Auerbach's plexus, which is present in at least some cases of cardiospasm.

In the absence of an anatomically demonstrable sphincter, Hurst visualizes a functional sphincter at the cardia, about one inch long, and situated entirely below the diaphragm. This corresponds with the observations of the absence of an anatomic sphincter, but a closed lower end of the esophagus, usually extending from the hiatus of the diaphragm to the cardia proper. If this theory is correct, this entire lower portion should be considered cardia, for the purpose of discussion, because it has a nerve supply the function of which differs from that of the rest of the esophagus.

The closed cardia in a patient with cardiospasm resists a water pressure of eight inches. According to Hurst,⁸ it is only when the column rises beyond this level that food is forced through the cardia and enters the stomach.

Heyrovsky¹⁰ states that the vagus not alone supplies the muscles of the esophagus, but also influences the tone of the cardia by contracting or relaxing it. One may, therefore, assume that in addition to atony of the esophagus, one may have not alone absence of normal relaxation of the cardia, but even increase of spasm beyond the normal. Much depends on whether the case is seen early or late in the disease.

A voluminous literature on cardiospasm has accumulated, dealing chiefly with its etiology. Much of it is confusing. The whole question of the etiology of cardiospasm requires further study, for the isolated clinical and experimental observations are still so much at variance, that no definite conclusions can be drawn. However, evidence is accumulating and appears quite conclusive that the condition is due to a neuromuscular dysfunction resulting from pathologic changes in the vagi, and more particularly in Auerbach's plexus. What these changes are due to, has not been determined. They may be of an inflammatory nature or the result of nutritional disturbance or avitaminosis. Recent investigations of cardiospasm have unearthed many facts that support the theory that nutritional and vitamin deficiencies play an important rôle in

the etiology It may be that all cases of cardiospasm are not due to the same etiologic factor, and, therefore, the inability to explain a particular case on the grounds of a nutritional or vitamin deficiency does not rule it out as an etiologic agent Cardiospasm is very common in some parts of Brazil, according to Etzel and Vasconcelos Etzel¹¹ observed 626 cases in an 18-year period, most of these cases came from rural districts of Brazil where the diet is poor and inadequate, and especially low in Vitamin B₁ The theory that cardiospasm is caused by a defect in the nerve plexuses did not explain the reason for these histologic findings The changes in Auerbach's plexus may be secondary to the nutritional and vitamin deficiency That cardiospasm is not due merely to local factors affecting the esophagus is suggested by Etzel's observation of the frequent association of cardiospasm or mega-esophagus with megacolon Etzel found that most of his Italian patients with mega-esophagus and megacolon came from a district in which pellagra is common

Cardiospasm has to be differentiated from other lesions producing obstruction at the cardia Benign stricture and carcinoma may be ruled out by the character and the duration of symptoms, combined with the roentgenologic appearance of the lesion The passage of a sound will aid Esophagoscopy examination, perhaps with a biopsy, will determine the diagnosis in doubtful cases The differential diagnosis between cardiospasm and other functional conditions affecting the lower end of the esophagus may be more difficult Spasm at the cardia may be secondary to an intra-abdominal lesion or a neurosis Diffuse spasm of the esophagus, which Vinson considers a definite entity, may simulate cardiospasm and is distinguished from it chiefly by sufficient spasm to prevent passage of a No. 60 F. sound into the stomach Esophagoscopy examination usually reveals tight contraction of the lower esophagus without a visible lumen Roentgenologic study shows diffuse contraction of the lower half of the esophagus Diffuse spasm of the esophagus may be secondary to a lesion of the abdomen Unless the removal of the intra-abdominal focus held responsible for the spasm relieves the condition, the treatment is the same as that for cardiospasm

Treatment of Cardiospasm—Most authors believe that spontaneous recovery never occurs, and, with our present knowledge, that there is no treatment which may be considered curative Once dilatation and hypertrophy have developed, the condition seems to be permanent The treatment is intended to relieve symptoms by improving drainage from the esophagus to the stomach The means to do this varies with the conception of the etiology If one considers spasm at the cardia to be the responsible factor, forcible stretching or dilation of the sphincter would naturally suggest itself as the treatment of choice In case one believes in the theory of achalasia, an attempt to rectify or overcome the responsible disturbed nervous mechanism is indicated After enormous dilatation of the esophagus has taken place, with elongation and sacculation, these secondary factors may be more important than the original achalasia or spasm, and require consideration of treatment from a different angle Without regard to etiology, however, there may be

another approach to the question of treatment and that is expediency and safety. It hardly seems justified to expose a patient to a serious and technically difficult operation if symptomatic relief may be obtained by a simple procedure.

While clinical and experimental investigations are being pursued, practical experience has shown that dilation of the cardia is followed by symptomatic relief.

The less severe cases usually remain under the care of an internist for a long time. Simple remedies are tried with more or less success. Many patients manage to get along fairly well by restricting their diet to bland liquids and soft food, others feel that solid food passes through more easily. Highly seasoned foods and those containing coarse particles usually have to be avoided. One has to be guided by the idiosyncrasies of the patients. They have to be cautioned to eat slowly, to take a small meal frequently, and to choose warm to cold food. Mild sedatives and antispasmodics may be of value. The simple passage of a stomach tube or bougie often brings temporary relief.

If these measures fail, or the condition becomes worse, more energetic treatment becomes indicated. It may be years before the symptoms become so severe that the patient is referred to an endoscopist or a surgeon. Without a definite understanding of the etiology, it has been found that mechanical forcible stretching of the lower end of the esophagus and cardia brings relief for shorter or longer periods. Many dilators have been designed and are in use. Vinson² begins with the passage of a No. 41 F sound passed over a previously swallowed twisted silk thread, and runs it up to No. 60 F. He states this mechanical dilation gives relief in about 10 per cent of cases, and that almost all of those having recurrences after this treatment, and the ones who are not benefited by it, can be cured by dilating the cardia with the Russel hydrostatic dilator. The risk of stretching the cardia with this expanding dilator after the passage of a No. 60 F sound is negligible.

Moore¹² starts treatment by passing mercury-filled bougies about once a week, beginning with the No. 28 F. This is done one-half hour after giving the patient 1½ gr nembutal and anesthetizing the throat with a spray of 2 per cent cocaine. If the patient tolerates the procedure well, he passes the next size, the No. 30 F. Each dilator is left in place about five minutes if possible. As the patients become more accustomed to the procedure, two can be passed each time. When the largest size, the No. 34 F, is reached, he encourages them to swallow the Mosher bag, and pumps it up to four pounds for five minutes. This produces a larger amount of stretching than is possible with the nonexpanding type of dilator but the bag is very difficult for some people to swallow. After the largest degree of dilation is reached, the patient is instructed to return when he feels the need of another dilation.

Mosher¹³ passes his pneumatic dilator under fluoroscopic guidance. The instrument is coated with barium. It is passed through the cardia, the position being judged by the appearance on the screen. When in place the usual inflation is carried out.

Jackson¹⁴ also uses the Mosher pneumatic dilator and stresses the importance of properly placing the instrument. At least the first dilation is done under the fluoroscope, so that an accurate measurement can be taken from the point of constriction to the upper teeth. To facilitate the taking of this measurement the dilator is calibrated in centimeters from the middle of its bag upward. When the apparatus is in such a position that, on inflation, the constriction of the bag is seen to be exactly in its middle, the measurement at the patient's upper teeth is read and recorded for subsequent placement of the dilator. The average measurement has been found to be 40 cm, the shortest 33 cm, and the longest 50 cm. In order to insure proper placement of the dilator some workers prefer to introduce it through an esophagoscope.

Once the dilation is accomplished, the after-treatment is quite important. It should be remembered that, especially in the long standing cases, the esophagus will be dilated and perhaps diseased. Therefore, careful regulation of the diet is indicated, no overloading of the esophagus may be permitted, and in some cases local treatment through the esophagus must be carried out. If the esophagus is very much dilated and constantly contains stagnated food remnants, daily irrigations with warm saline solution are very beneficial.

Occasionally, the dilatation and distortion of the esophagus will be so great that no thread will go through to be used for the passage of a bougie. On esophagoscopy the attempt to find the cardia may also be unsuccessful. Under such circumstances, if dysphagia is severe, a gastrostomy is indicated in order to permit correction of the hunger and dehydration. Once these symptoms are overcome one of several plans may be adopted. At times, it has been found feasible to carry out manual dilatation of the cardia from below. If this cannot be done, a retrograde esophagoscopy may be performed. Once the passageway has been found, a bougie is passed upward to the mouth. This is used to draw a thread into the stomach, and out through the abdominal wound. The thread is then kept in place and used either for retrograde bouginage or for guiding bougies passed from the mouth as recommended by Plummet¹⁵.

In the great majority of cases symptomatic relief can be obtained by the methods of dilation just described without great risk to the patient. In case of failure, or because of severity of symptoms, operation may be considered.

Some authors have never found it necessary to operate. Gray and Skinner¹⁶ stated recently, that in over 1,200 cases of cardiospasm seen at the Mayo Clinic operations for the relief of cardiospasm were performed only seven times. The procedures consisted of the Mikulicz operation of manual dilation of the cardia, four times, esophagogastricostomy, once, thoracocervical sympathectomy, once, and abdominal sympathectomy combined with manual dilation of the cardia, once.

Operation is undertaken only for a very definite indication.

- (1) To bring about relief in those cases in which dilation has failed
- (2) In the hope of bringing about more permanent symptomatic relief than is usually obtained after instrumental dilation
- (3) To try to remedy the cause of the disability

The simplest operations are those designed for symptomatic relief by establishing better drainage of the esophagus. Various procedures have been devised, some of which have been given up because they proved dangerous or ineffective. Those most commonly employed at the present time are freeing of the cardia and lower esophagus, combined with instrumental dilation from above, manual dilation from below through a gastrotomy, or transperitoneal esophagogastriostomy.

To expose the region an epigastric incision is made just to the left of the median line and carried upward into the angle between the ensiform and the costal margin. It is rarely necessary to perform an osteoplastic resection of the costal arch. The left lateral ligament of the liver is divided and the under surface of the diaphragm exposed. Eggers¹⁷ operated upon three cases by this method. The cardia and the lower esophagus were completely freed out of their bed. A tape was passed around the esophagus and all connective tissue strands, blood vessels and nerve fibers surrounding it were divided until the longitudinal fibers of the esophagus could be followed down onto the wall of the stomach. By gentle traction the esophagus could be palpated well up into the mediastinum. There was no abnormal thickening or infiltration noted. The wall was soft throughout and there was no sudden transition from the dilated to the narrow portion, or at the entrance of the esophagus into the stomach. A large stomach tube was passed without difficulty. Exploration of the abdomen revealed extensive adhesions from former operations in one case, and an old duodenal ulcer and a patent gastro-enterostomy in another case. Whether they could be held responsible as etiologic factors is questionable. In one patient, Eggers performed a gastrotomy and manual dilation of the cardia in addition to the above procedure. A one-inch incision was made in the anterior wall of the stomach between traction sutures. The stomach was emptied by means of suction, and a finger then inserted for exploration of the cardia. A small dimple was felt but the finger did not enter the esophagus until gradual pressure had been exerted. The index finger was inserted and then the middle finger. The cardia was stretched in all directions until it admitted two fingers. Stretching with two fingers simultaneously was not very successful on account of the depth. Considerable food remnants were found in the esophagus in spite of the fact that it had been irrigated prior to operation. These were removed by suction. The incision in the stomach was closed with two rows of sutures. The convalescence was uneventful. This patient was entirely relieved of all his symptoms, and gained 30 pounds in weight. Re-examination of his esophagus, three years later, showed the condition of the esophagus to be unchanged, with identical roentgenologic evidence of cardiospasm, and no diminution in the size of the esophagus in spite of complete symptomatic relief (Fig. 4).

Several authors have commented on similar observations, notably Stubbe¹⁸ and Stephens¹⁹. The latter reported ten cases treated with dilation, in only two of which decrease in size of the esophagus was noted. There is at present no adequate explanation for the symptomatic relief without appreciable change

in the roentgenographic appearance of the esophagus. One is forced to the conclusion that the mechanical dilation does not "cure" the condition, but simply results in diminishing the resistance of the cardiac sphincter to the passage of food.

In patients with marked elongation and sacculation of the esophagus, in whom the secondary mechanical factors are perhaps more important than the



FIG 4—1935—Cardiospasm before operation
1938—Cardiospasm three years after manual dilation of cardia. Complete symptomatic relief with gain of 30 lbs in weight. Roentgenologic appearance of esophagus unchanged.

original achalasia, esophagogastrostomy offers the best results. It may be performed through the thorax, but has been given up by most surgeons because of inaccessibility or danger of empyema. Heyrovsky¹⁰ is credited with the development of the operation by the abdominal route. Collected statistics by Fromme,²⁰ and Haggstrom²¹ show a negligible mortality, and good functional results. After freeing the cardia and esophagus through a high epigastric incision as described, the dilated portion must be drawn down through the hiatus before an anastomosis can be safely performed. The hiatus may have to be widened and the crura of the diaphragm divided. Several operations employing a technic similar to Finney's pyloroplasty have been described within the last few years. Churchill,²² and Womack²³ have each reported successful cases. The operation should be considered a serious one and not be undertaken lightly. It finds its greatest application in patients whose esophagus is elongated and sacculated.

Longitudinal incision of the musculature similar to Rammstedt's operation on the pylorus has been recommended by Heller,²⁴ and favorable results have

been reported by numerous writers. The many observations of the absence of an anatomic sphincter, or any abnormal thickening, make it appear that there is no indication for a plastic procedure, and that an incision of the musculature carries the risk of perforation.

Operations aimed not alone at symptomatic relief, but which are intended to try to remedy the cause of the disability have been developed since the experimental work of Hurst,^{8, 25} and Knight,³ and others, called attention to the importance of disturbances of the neuromuscular mechanism of the cardia in the production of cardiospasm or achalasia. Knight himself performed the operation, based upon his experimental work, on four patients, but the results do not seem to have been as satisfactory as had been anticipated. W. A. D. Adamson, of the Royal Infirmary, Edinburgh, and G. E. Gack of St. Bartholomew's Hospital, London, have each performed the operation upon four patients (quoted by Knight³), in none of these are late reports available. In this country, Eliason and Erb²⁶ have operated upon two cases by the method advocated by Knight. A sympathetic denervation of the cardia was undertaken by excising a portion of the left gastric artery with its surrounding fat and nervous tissue. The first case was materially benefited, symptomatically, the second one, to a lesser degree. In neither case was the size of the esophagus perceptibly reduced.

Craig, Moersch and Vinson,²⁷ of the Mayo Clinic, performed a bilateral resection of the cervicothoracic trunk and ganglia, in a patient in whom ordinary methods of treatment had failed, and in whom dysphagia and severe pain were the outstanding symptoms. Preliminary tests were made which indicated to the authors that permanent relief of pain might be effected following removal of the sympathetic ganglia. Posteromedian incisions were made extending from the tip of the fifth cervical spine to the tip of the fourth thoracic spine. After resecting a portion of the transverse process and the first rib the posterior mediastinum was entered. The cervicothoracic sympathetic trunk and ganglia were removed on both sides. A bilateral operation was performed more fully to denervate the esophagus and to equalize the rise in surface temperature of the skin of both arms and both sides of the face. From a cosmetic standpoint also, the bilateral operation is preferable since it produces a bilateral Horner's syndrome. The patient's postoperative course was uneventful, and the wound healed perfectly. Following operation, she was completely relieved of dysphagia, and of the residual type of pain, and she has had no further paroxysmal attacks of the acute type of pain.

With the present state of our knowledge and on the evidence submitted so far, it does not seem justified to advocate extensive operations on the sympathetic nervous system. As Bird²⁸ states, from the work of some of these authors it seems unlikely that any operation of reasonable magnitude will effectively remove the sympathetic supply to the cardia. Furthermore, it seems doubtful that denervation will benefit patients with advanced degrees of the disease in which the mechanical factors are prominent. Instrumental dilation offers the best chance of relief in the majority of cases. Only on those in whom it

fails or who are too far advanced may one of the procedures aimed at establishing better drainage be instituted

From a study of the modern literature one gains the impression that a disturbance of the neuromuscular mechanism of the esophagus and more particularly of the cardia, is responsible for the symptom-complex of cardiospasm. There is no other way to explain the diffuse dilatation with obstruction at the lower end in the absence of an anatomic sphincter. No other esophageal obstructions, whether due to carcinoma, fibrous stricture, or other lesions of long duration are associated with nearly the degree of dilatation which is observed in cardiospasm. The fact that in the great majority of cases the esophagus does not return to normal after establishing improved drainage, likewise, supports this view. One has to assume the existence of a nerve lesion which affects the fibers of the esophagus itself and permits dilatation, and at the same time keeps the cardiac end closed, whether by spasm or achalasia.

If this conception is correct, one is justified in the assumption that the disease which causes cardiospasm probably has preceded the fully developed condition for which the patient is referred to an endoscopist or a surgeon. It may be a terminal condition in which the greater amount of damage to the nerve mechanism has already been done. One may liken it to acute poliomyelitis, in which the acute disease of the spinal cord is of short duration and has usually subsided at the time neurologists and orthopedists are called in to treat the resultant damage.

Assuming this course of events, it becomes evident that any treatment intended to be curative, would have to be administered earlier than is now usually the case. We should know the underlying etiologic factor causing the neuromuscular disturbance, whether it be inflammatory or nutritional. Deficiency of Vitamin B₁ has been held by some writers to be responsible. It is along this line that profitable research may be directed.

In the meantime, symptomatic relief can be brought to the great majority of patients by means of dilation of the cardia, either mechanical, from above, or rarely, manual, from below. Neither procedure entails any undue risk.

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THE MANAGEMENT OF APPENDICEAL PERITONITIS—WITH SPECIAL REFERENCE TO THE OPERATIVE HANDLING OF THE LOCALIZED ABSCESS

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SINCE the original paper on the deferred treatment of peritonitis of appendiceal origin by A J Ochsner¹ there has been a rather intense controversy on this subject. It is safe to say that most observers have seen fit to reject his ideas altogether, but some have accepted them and have applied them with considerable success. This latter group, during recent years, has been able to win adherents by their continual insistence that there is a great deal of virtue to the deferred treatment when applied to particular cases of appendiceal disease, specifically the ruptured group and more specifically certain well-defined cases of the ruptured group. We shall attempt to define the groups in which we believe a gratifying reduction in mortality can be brought about.

Interpretation of the Ochsner Treatment—Some of the difficulty encountered by advocates of the deferred treatment in discussing their views has come from the variety of interpretation put upon the Ochsner treatment. We find, in interviewing many observers and in reviewing the literature, that there is little uniformity of interpretation. A clear-cut definition of Ochsner's¹ idea may be found in a few words in his "Handbook of Appendicitis." He states "The temperature was 104° F, pulse 140, abdomen enormously distended, features pinched. My experience with this and similar cases had taught me that whenever I operated upon patients approximately in this condition, the patient invariably died."

"Some years ago, before I had learned to appreciate the treatment which I describe, I frequently operated upon patients in just this condition as a last resort, thinking that this gave them the only possible chance of recovery. Since then I have learned that this case belonged to a class which practically never recovered after an operation, if it is performed while the condition is that in which I found this patient, and of which a very large majority recover if the treatment (delayed) is followed which I have described —"

These statements represent the basic idea of his principle, and there has been no divergence from this principle by his modern day adherents. Changes in this principle, if they have been made, are in the nature of refinements of application of this basic fundamental. We shall attempt to clarify some of these refinements. Let us make it clear in the beginning that we believe that there can be no contention over the idea that immediate operation is the only form of treatment for acute, unruptured appendices. Though it may be deemed unnecessary, we make this statement especially strong because there are some who believe that the advocates of the deferred treatment would defer operation in all cases of appendicitis. If cases of appendicitis presented them-

APPENDICEAL PERITONITIS

selves and were operated upon before rupture occurred there would be no need for the discussion we are now presenting. We are still faced with the fact, in spite of intensive public education, that Bowe² in 5,000 cases found that 44 per cent of patients suffering from appendicitis have peritonitis on admission to a hospital. Foss³ encountered 46.5 per cent of peritonitis in

FIG 1

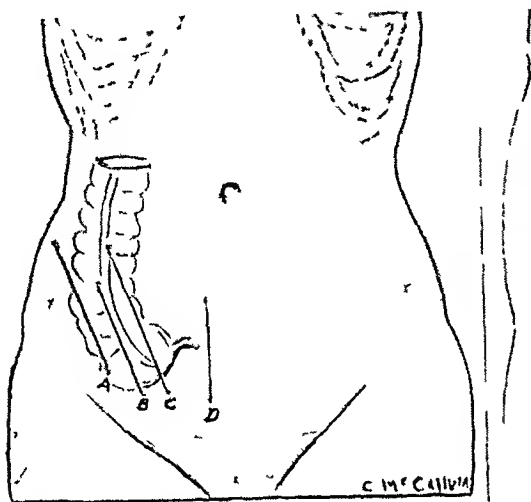


FIG 2

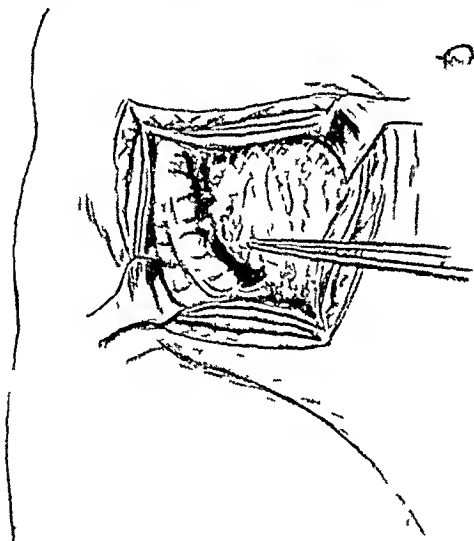
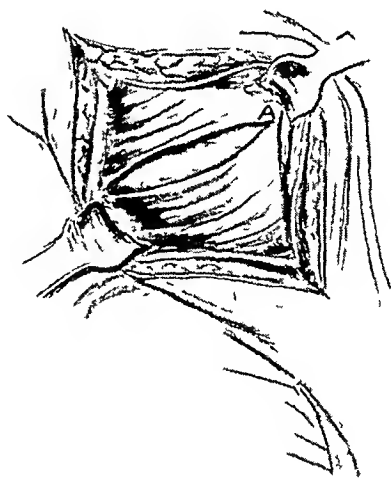


FIG 3

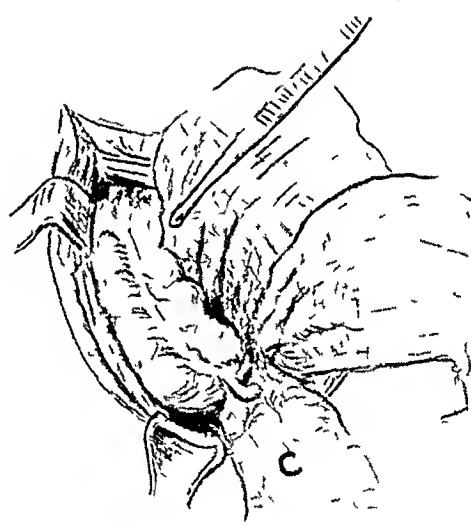


FIG 4

FIG 1—The location of some of the incisions used in cases of abscess. Incision B is probably the one most commonly required. The variation in the situation of these incisions serves to illustrate the point that strict individualization is the most important factor in the selection of site of incision.

FIG 2—Illustrating the degree of exposure which should be obtained if the incision is adequate.

FIG 3—Illustrating the extreme degree of exposure of the contents of the right lower quadrant which it is possible to obtain through an "extensive" McBurney incision.

FIG 4—This is a complementary illustration to Figure 3, and shows the use of Mikulicz pads to exteriorize the cecum and abscess.

1,000 cases on admission to the hospital. Keyes⁴ found that 50.3 per cent of 495 cases had peritonitis on admission to the hospital. Alton Ochsner⁵ reports the astounding percentage of 78.7 in a series at Charity Hospital in New Orleans. So with Hamilton Bailey⁶ we say that, "With the advent of that Elysium when all cases of acute appendicitis are in the hands of the surgeon when the disease is still limited to the appendix the need for the Ochsner (delayed) treatment will pass."

The interpretation put upon the Ochsner treatment in England, by Sherren,⁷ was that all ruptured cases should be deferred, even those with a localized abscess, until complete resolution had taken place and recommended removal of the appendix during a "well interval" several months after resolution. Of course, he and his adherents encountered cases in which resolution

FIG 5

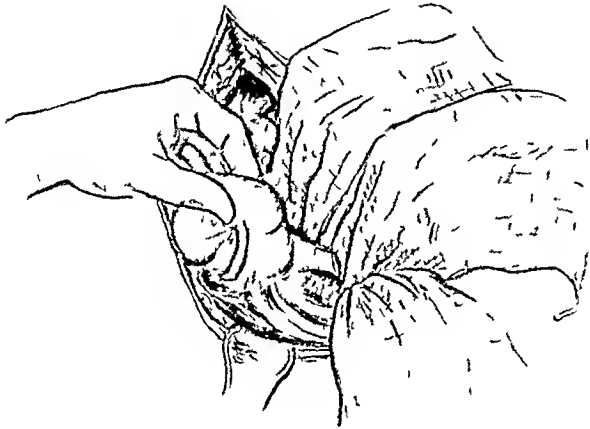


FIG 6

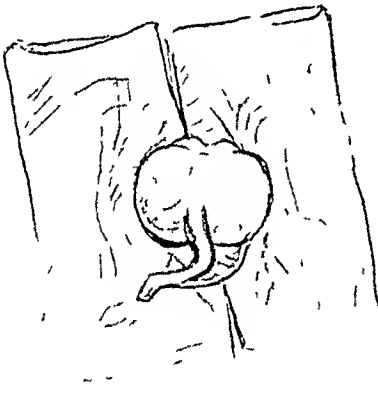
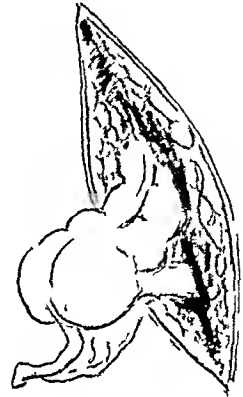


FIG 7

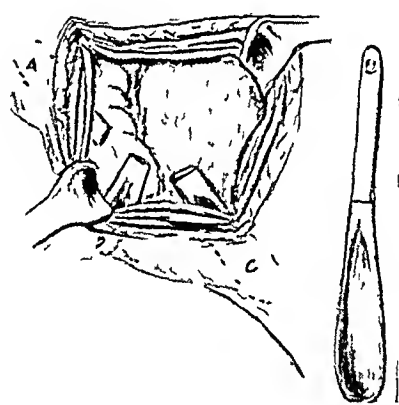


FIG 8

FIG 5—Illustrating the exposure of an appendix lying directly posterior to the head of the cecum. The exposure is accomplished by rotation of the head of the cecum forward.

FIG 6—Illustrating the delivery of the head of the cecum with the appendix from the abdominal cavity. This degree of motility is frequently attainable especially in thin or viscerotonic subjects. Delivery of the cecal head with the appendix is attainable in the large majority of patients.

FIG 7—Illustrating the exteriorization of the operative field with gauze pads after delivery of the cecum and appendix. This affords protection against soiling in the event that the appendix is ruptured during removal in the acute, nonruptured cases.

FIG 8—It will be noted that the omentum has been tucked down around the medial aspect of the head of the cecum and over the small intestine down on to and over the brim of the pelvis. All drains are placed exterior to this omental 'sheet'.

would not take place, and in these instances incision and drainage of the abscess was recommended with removal of the appendix sometime later. This same interpretation has been applied by men in this country with a reduction in their mortality. At another extreme, some have applied the deferred treatment to a restricted group which includes only those cases in shock or near *extremis*, with an acute peritonitis, in whom supportive treatment

is given until the general condition of the patient can be improved somewhat, but waiting is not continued until localization of the peritonitis before operative intervention. Our position is a sort of middle ground. We have found through experience that cases with diffuse peritonitis will go on to localization if they can be tided over the period of profound toxemia, and,

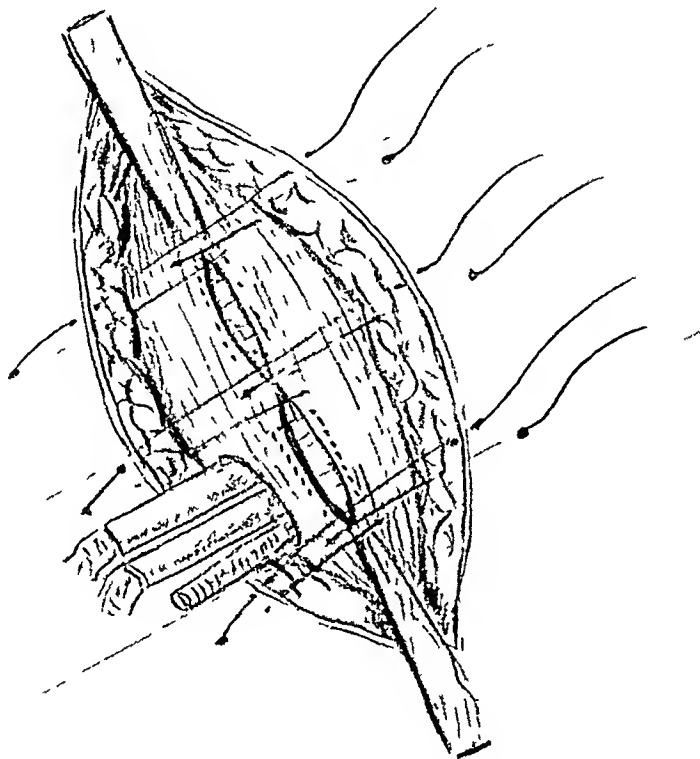


FIG 9 —Illustrating the closure of the external oblique fascia and skin

therefore, we wait for this localization. However, we do not go so far as the Shellen group. We do not wait for complete resolution of a localized abscess, but prefer to operate during the stage of abscess. We adhere to this latter idea because we believe that the waiting necessary for complete resolution carries a patient into the period of danger from ascension of infection through the portal system, spontaneous rupture of a distended abscess cavity through its protective wall into the general cavity, septicemia, and other complications attendant upon the prolonged presence of an abscess anywhere in the body. We are certain that the reason for very prolonged waiting is, as Biaddon⁸ puts it, the fear of "the tragedy of conversion of a localized abscess into a general peritonitis." The mortality produced by prolonged waiting overbalances the mortality in our series of abscess cases which have been operated upon. Since this experience has not been universal, we have been

forced to the conclusion that there must be some particular virtue in our method of handling the abscess case. We have, therefore, incorporated a detailed description of the operative technic employed by us in this group in the discussion of the deferred treatment, because, we cannot help but believe that it has served as a very important part and parcel of the results accomplished by us with the deferred treatment.

Rationalizing the Principle of Waiting—The principle of deferred operation has a great deal of precedent in the handling of other surgical conditions. The ideas to which we now adhere so strongly in regard to the management of empyema, gonococcic infection of the fallopian tubes, and infections of the hand with lymphangitis, were arrived at through a long process of trial and error and through antagonism almost as intense as that against the deferred treatment of the ruptured appendix. It was not until the experience in the handling of empyema which the World War afforded, that we became convinced that the proper method of treating a pleural effusion following pneumonia was to wait until the acute exudative process was over, the pus in the pleural cavity had become thick, and the patient had been allowed to develop some immunity to the infection. Early in this century an acute gonococcic infection of the tubes and adjacent pelvic peritoneum was considered ripe for immediate operation. Through a gradual process of study we have now come to the opposite conclusion—that operation should be delayed in gonococcic pelvic inflammatory disease. We have learned that immunity will be established, and that the patient is a much less serious operative risk during a more quiescent stage of the disease. Infections of the hand with lymphangitis, are now deferred until localization is complete, and some immunity is established.

Comparative statistics of our own appeal to us convincing. In a series of 94 cases with diffuse peritonitis, which were immediately operated upon, ten died, a mortality of 10.64 per cent. In 139 cases of acute diffuse peritonitis treated conservatively and operated upon later, there were two deaths, a mortality rate of 1.43 per cent. We feel that this comparison alone should serve to lift the proposition of deferred treatment from the category of supposition to the realm of established fact. Collier and Potter⁹ report their mortality rate in acute appendiceal peritonitis with immediate operation as 52 per cent. With the adoption of the deferred treatment they were able to reduce their mortality to 8.6 per cent. This is the most striking statistical evidence we have discovered. Deaver and Magoun¹⁰ report 1,358 cases of acute appendicitis operated upon between the years 1901 and 1905 with a mortality rate of 10.5 per cent. In all of these cases the patient was immediately operated upon when seen. In 1910, the deferred treatment was adopted for all indicated cases, and from 1910 to 1914 there were 1,385 cases with 52 deaths, a 3.7 per cent mortality. Walker¹¹ reports a series of 30 cases treated by deferred operation with four deaths, a mortality of 13 per cent, and compares it with a mortality of 42 per cent in 77 cases treated by immediate operation.

Technic of Waiting.—As was stated above, we advocate deferring operation in those cases who are first seen when they are in a stage of diffuse peritonitis. This condition may be present (1) A few hours after onset of appendiceal disease in those cases which go on to perforation rapidly, (2) in some cases many days after the onset of appendiceal disease where the perforation was successfully localized immediately, but continued growth of the abscess has allowed it to break through its protecting barriers into the general peritoneal cavity, (3) those cases in which evidence of diffuse peritonitis appears three to four days after onset of appendiceal disease. Parenthetically, we may say that the latter group is the most common one, but we would like to deemphasize the phrase "third to fourth day cases" which so commonly appears in the literature. This phrase is confusing because it denotes a rule of thumb in a condition where strict individualization of cases is necessary. As we shall go on to show and attempt to illustrate, the deferred treatment is indicated in all cases of rupture with diffuse peritonitis whether this complication has supervened hours, days, or weeks after the onset of symptoms.

Operation in either of the three groups cited should be deferred until evidence of localization takes place. The symptoms of peritonitis, distended and rigid abdomen, rapid pulse, high temperature, prostration, and hippocratic facies will gradually disappear in the course of a few days, and the patient will present a picture of localized abscess and satisfactory general physical status. When this latter status is accomplished, operative drainage of the abscess and removal of the appendix is indicated. Let us state again that, contrary to the attitude of some advocates of the Ochsner principle, we do not wait for complete resolution of the abscess. We realize fully that this resolution will take place in the majority of cases, but this prolonged waiting is fraught with danger of complications far greater than the danger of a gently and expeditiously executed operation upon the abscess. The above three groups are the only ones in which we believe that operation should be deferred for any appreciable length of time. There are many cases that when first seen have some suspicious evidence of perforation but in whom the evidence of peritoneal irritation is local. These cases should not be deferred. Cases where one can be reasonably certain that perforation has taken place recently but the signs of peritonitis are local should not be deferred. Cases which are first seen after a localized abscess has definitely formed should not be deferred. The citation of illustrative cases will serve to clarify the statements of this paragraph, and also give a more concrete and workable knowledge for use in individualizing cases.

ILLUSTRATIVE CASE REPORTS

Case 1—J. G., male, age 17, was admitted to Columbia Hospital, October 15, 1937, stating that generalized abdominal cramps had begun three hours before admission. He took a large dose of epsom salts on his own initiative shortly after these pains began. At the time of admission his temperature was 103.5° F, pulse 110, the abdomen markedly distended, tender and rigid throughout. The facial expression was typically

"washed-out" He was vomiting frequently and profusely. Intravenous saline and glucose were begun and administered in adequate amounts for six days (The continuous intravenous drip serves admirably to furnish fluids to these patients over a period of days) A Bartlett apparatus attached to a Levine tube in the stomach was used for continuous decompression. Large doses of morphine were given as indicated for pain and restlessness. Six days after admission the temperature was 100° F, the pulse rate normal, the facial expression good, and the distention, generalized rigidity and tenderness had disappeared. The intravenous fluids and continuous gastric suction were discontinued and he was able to take fluids and a light diet. A palpable mass was apparent in the right lower quadrant, and rectal examination revealed an inflammatory mass in the cul-de-sac (The appearance of diarrhea in patients with peritoneal suppuration so frequently indicates a cul-de-sac accumulation. Rectal examinations should be made at indicated intervals to aid in determining the operative approach) On October 26, 1937, operation was performed through a low, extensive McBurney incision. The appendix was removed and the cul-de-sac abscess and that in R L Q were drained. The postoperative course was relatively uneventful.

This case is cited to illustrate some features of the supportive treatment of patients during the process of waiting, but more particularly to illustrate the possible sudden onset of evidence of general peritonitis with its accompanying prostration. This patient had been suffering with abdominal pain only three hours before he was first seen. Such rapid progress of appendiceal disease to the point of rupture and general peritonitis is unusual.

Case 2—J. E., male, age 16, was admitted to Columbia Hospital, February 5, 1935, with a history of abdominal discomfort beginning three days previously. The pain became progressively worse and he had become distressingly sick during the previous 12 hours. Vomiting had been prominent, and at the time of admission to the hospital the temperature was 103° F, pulse 130. The abdomen was distended and rigid. The facies bespoke the profoundness of the toxemia. He was vomiting copiously at frequent intervals. Treatment was instituted along the same lines described in Case 1. During the course of the next four days the evidences of profound toxemia disappeared, and a localized mass became palpable in the R L Q. After two more days localization was considered complete and operation upon the abscess performed.

This case is typical of those referred to in the literature as "third to fourth day" cases. This one was deferred because the evidence of profound toxemia had supervened and not because of the duration of the disease. The former should invariably be used as the criterion for deferring operation instead of the latter. Waiting should not last longer than the time necessary for localization and cessation of extreme toxemia to take place.

When speaking to the skeptical about the deferring of operation the question is quite naturally asked, "how many patients die while one is waiting?" In the series here reported, which includes 131 cases of acute diffuse peritonitis with profound toxemia, two died, a mortality of 1.52 per cent. This figure is measurably lower than those of observers advocating other methods whose material we have studied in the literature for comparison. The small percentage of mortality during the process of waiting seems to weigh heavily in favor of our contention. It may be compared with our figure of 10.75 per cent, Collier's⁹ 52 per cent, and Walker's¹¹ 42 per cent in cases operated upon immediately.

Case 3—B H J, female, age 9, was admitted to Columbia Hospital, July 3, 1938, stating that abdominal pain had begun on June 29, 1938. Nausea and vomiting were not associated, and she was not incapacitated until July 2, 1938, when she was referred to the hospital. Examination revealed a palpable mass in the R L Q, with no abdominal distention. The temperature was 103° F, but the facial expression was good and general physical status excellent. With a diagnosis of appendiceal rupture, with abscess formation, operation was performed on the day of admission. An extensive McBurney incision was employed, the appendix removed, and the abscess drained. The postoperative course was relatively uneventful.

This case serves to illustrate that waiting is not practiced where localization has already taken place and the physical status of the patient is good. It also serves to illustrate that large group of cases in which rupture occurs and in which there is never any evidence of general peritoneal soiling. The omentum and anatomic position of the appendix, and slowness of spillage serve to keep the process localized from the very beginning. Other cases of this type will be cited for other features pertinent to the discussion.

Case 4—H S, female, age 9, was admitted to Columbia Hospital, July 7, 1938, with a history of vague abdominal pain of 24 hours duration. Associated diarrhea at the onset suggested a diagnosis of gastro-enteritis to her attending physician, and a definite diagnosis of appendicitis was not made until about 18 hours after onset of pain. Physical examination revealed a child in good general condition, with marked tenderness and rigidity in the R L Q. No distention or other evidence of diffuse spread was present. Temperature 101.5° F, pulse 110. A definite diagnosis of appendicitis could be made but the fact that rupture had occurred could be and was questioned. Operation was performed on the day of admission. Fluid with a distinct colon odor was found upon opening the abdomen through a McBurney incision. The appendix was found to be perforated near its tip with spillage fairly well walled-off by plastic lymph and omental adhesions. The appendix was removed and the abscess thoroughly drained.

This case was chosen because it is characteristic of that large group in which one may entertain considerable doubt that the appendix has ruptured. There is no reason to delay operation on these cases. Cases of this type have given rise to more contention than any other group, and serve as the main reason that a great many surgeons feel that they cannot accept the deferred treatment. This contention has been caused more by misunderstanding than by disagreement.

Two cases (Nos 5 and 6) have been taken from our files to illustrate our belief that prolonged waiting for resolution of the abscess is dangerous.

Case 5—W C, male, age 13, was admitted to Columbia Hospital, September 23, 1938, with the history that six weeks before admission he had suffered an attack of abdominal pain, with nausea and vomiting which cleared up to some extent although he had been incapacitated for work or play since the onset. Three days before admission he became acutely ill again and arrived at the hospital *in extremis*. He was intensely jaundiced, the abdomen was markedly distended and tender. He expired two days after admission. No operative procedure was attempted because of his very poor general condition. Autopsy revealed a ruptured, gangrenous appendix, with a huge pelvic abscess which had ruptured into the general peritoneal cavity, a blood stream infection with metastatic lung abscess, acute vegetative mitral valvular endocarditis, and marked cloudy swelling of the liver.

This case illustrates the danger of leaving an abscess of appendiceal origin for a prolonged period. This patient's outlook for recovery would have been good if he had presented himself a few days after rupture, or even a week or ten days before he did apply for treatment. As we have stated, there is a considerable amount of literature appearing to-day which tends toward the attitude that prolonged waiting for complete resolution is the procedure of choice. We voice the result of our experience that it is a procedure the danger of which greatly outweighs that of a properly executed operation upon the well-formed abscess. The English advocates of prolonged waiting state that the unfavorable eventualities can be obviated by observing these patients in "the very shadow of the operating amphitheatre", but we find it difficult to conceive of them being able to recognize an "impending" spread of the infection into the blood stream or the rupture of a culdesac abscess into the general cavity. One of our colleagues has observed the rupture of a cul-de-sac abscess during abdominorectal examination.

Case 6—H. B., male, age 21, was admitted to Columbia Hospital, August 8, 1938, with a definite history of an acute attack of appendicitis four weeks previously. He assumed that the attack had subsided uneventfully when the nausea, vomiting and severe abdominal pain disappeared. He continued his participation in the activities of a summer camp until a few days before admission, when he noticed a tender mass in his right lower quadrant. (This is not unusual, we see an occasional patient who is ambulatory with a circumscribed appendiceal abscess.) At operation he was found to have a well-defined appendiceal abscess. There was also extensive destruction of the head of the cecum, which feature makes this a case in point. It was necessary to resect a part of the cecum to get above this diseased portion. He developed a cecal fistula which has just been closed at the time of this writing, one year later. We attribute the destruction of the head of the cecum to the fact that the infection was allowed to dissect between the layers of the cecum. We have seen this condition in other cases which were allowed to wait for prolonged periods.

We believe that the two cases above cited illustrate adequately the danger of prolonged waiting, which leads one to the belief that this danger is more real than imagined. We would like to avoid being controversial on the issue of prolonged waiting. We accept the fact that all but about 25 per cent of cases with appendiceal peritonitis will go on to complete resolution. It is in this remaining 25 per cent where operation is "forced" (Lehman¹²) that the danger of complications which we have described outweighs the danger of operating upon a well-circumscribed abscess, when it appears. This should not be made an issue among those advocating the deferred treatment because it detracts from the strength of their stand on the main issue, that is, the deferring of operation upon the patient with diffuse peritonitis until he has been tided over the "critical" stage of his illness.

Technic of Operation upon Appendiceal Abscess—We go into some detail, perhaps unnecessarily, in the accompanying illustrations in an attempt to define the operative approach and handling of appendiceal abscess. We feel that this type of surgery, like any other, depends in large part for its success on scrupulous attention to detail. First, the location of the incision should

be made directly over the abscess to avoid traversing unsoiled viscera as much as possible. Second, the extent of the incision should provide adequate working room to promote gentleness and facility of execution of subsequent steps. Third, mobilization of the head of the cecum is important. We emphasize this because this maneuver relieves us of the necessity of "rooting" for the appendix, removing it retrograde, and using other procedures which bespeak inadequate "control" of the operative field. Fourth, the adjacent areas should be protected from soiling. The necessity for this is evident, we have attempted to describe its accomplishment in the legends. Fifth, adequate drainage should be employed. For this purpose we use cigarette and split, fenestrated soft rubber tubing which is never placed between coils of small intestine. Sixth, the placing of the omentum preliminary to closure is highly important. This should be done so that the abscess area is exteriorized as much as possible, and so that the drains are not in contact with the small intestine. Seventh, the closure of the wound is done loosely. The wound is always potentially, if not actually, infected. By delivering the drains through stab wounds we try to avoid the occurrence of postoperative hernia.

TABLE I
SUMMARY OF MORTALITY STATISTICS IN 3,795 CASES OF APPENDICITIS

	No of Cases	No of Deaths	Mortality Percentage
(1) Recurrent appendicitis	1,572	0	0
(2) Acute appendicitis	989	1	0.10
(3) Acute gangrenous ruptured appendix with localized abscess	545	3	0.55
(4) { Acute gangrenous ruptured appendix, with diffuse peritonitis —immediate operation	94	10	10.64
(5) { Acute gangrenous ruptured appendix with diffuse peritonitis —deferred operation	139	2	1.43
(6) <i>In extremis</i> —drainage—appendix not removed	12	3	25
(7) Appendix removed in course of other operations	444	0	0
Totals	3,795	19	0.50

SUMMARY AND CONCLUSIONS

(1) Attention is called to the fact that the statistics detailed in Table I show the mortality incidence in a continuous, consecutive, unselected series of cases of appendicitis, extending over a period of more than 35 years. During this period a mortality of around one-half of one per cent has been sustained. A fact which, in itself, is most significant.

(2) We regard the deferred treatment in the cases in which it is indicated as the first step in the operative procedure, and in no way is it regarded as a substitute for operation.

(3) There is abundant evidence, both clinical and experimental, to prove the unmistakable tendency toward localization in cases of appendicitis complicated by the presence of pus.

(4) There is an optimum time for operating upon every surgical patient. The great problem of surgical judgment is to be able to select that time.

The greatest ally the surgeon has in these critically ill patients is their amazing defense mechanism

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BILE PERITONITIS

REPORT OF EIGHT CASES

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BILE PERITONITIS is the resultant peritoneal reaction caused by a variable amount of free bile within the peritoneal cavity. During the past 40 years, German and French observers have published on this topic a very extensive literature dealing, primarily, with the so-called idiopathic types of biliary peritonitis. Since 1920, a number of American investigators have reported observations on experimentally produced bile peritonitis in animals, but American and British literature still contains little on the clinical aspects of this condition. For example, two monographs on diseases of the liver and biliary tract by American authors, published in the past fifteen years, have no reference to bile peritonitis.

The treatment of eight such cases during the past six years, together with a detailed investigation of this subject, forms the basis of this paper.

CASE REPORTS

Case 1—A male, age 68, was admitted to the University Hospital, with a slight clinical jaundice, and a history of recurrent calculous cholecystitis. The gallbladder was not visualized roentgenologically. Calculous cholecystitis was demonstrated at operation, the common duct was normal. A cholecystectomy without drainage was performed. Convalescence was stormy and lobar atelectasis, abdominal distension, and ascites developed. On the twelfth postoperative day a small incision was made in the right lower quadrant. Normal appearing bile drained copiously for two weeks, but gradually ceased by the twentieth day. On the fortieth postoperative day a right subdiaphragmatic abscess was evacuated of two liters of infected bile. Recovery was prompt, and the patient was discharged on the seventy-sixth day.

Case 2—A female, age 76, was admitted to the University Hospital, with a history of recurrent calculous cholecystitis over a period of 30 years. Jaundice had occasionally been present, the attacks accompanied by chills and fever. Jaundice was not present on admission. No gallbladder shadow could be demonstrated roentgenologically. Chronic calculous cholecystitis was found at operation. The common duct was not dilated and no stones were palpated. Cholecystectomy was performed, with drainage of the gallbladder fossa. Twenty-four hours later abdominal pain, distension, fever and tachycardia developed, and profuse drainage of bile was noted along the abdominal drain. The patient appeared gravely ill and failed rapidly, she expired 48 hours postoperative. Post-mortem examination disclosed 1,000 cc of bile in the peritoneal cavity. A stone one centimeter in diameter was firmly impacted in the ampulla of Vater. No definite site of perforation was demonstrable in the common duct, cystic duct stump, or gallbladder fossa. *Pathologic Diagnoses* Bile peritonitis, common duct stone, and pulmonary atelectasis.

Case 3—A female, age 48, was admitted to the Methodist Hospital, with acute calculous cholecystitis of three days' duration. Exploration revealed an empyema of the gallbladder, with beginning gangrene of the wall. A cholecystostomy was performed, no stones were found in the gallbladder. The patient made a satisfactory recovery except

for a persistent mucous fistula Six months later a cholecystectomy was performed and a stone found firmly lodged in the ampulla of the gallbladder The common duct was not enlarged and no stones were palpable in it The gallbladder fossa was drained Sixty hours later abdominal pain, distension, fever, and tachycardia abruptly developed, and the patient appeared to be in surgical shock There was profuse drainage of bile along the abdominal drain Rapid circulatory failure followed, with death 18 hours after onset of the complication No postmortem examination was permitted, but death certainly was due to bile peritonitis, resultant either from a slipped cystic duct ligature or an overlooked common duct stone, with perforation of the biliary tree

Case 4—A female, age 53, was admitted to the Immanuel Hospital, with a history of chronic calculous cholecystitis of ten years' duration, but with no jaundice The gallbladder was not visible roentgenologically A chronically diseased gallbladder was found at operation, with a stone firmly impacted in a very short cystic duct Cholecystectomy was carried out, and the cystic duct stone removed A small incision made in the common duct, to permit removal of the stone, was closed with interrupted sutures The abdomen was closed, with drainage Thirty-six hours later a definite and rapidly increasing tachycardia developed, the pulse increased gradually from 100 to 170, with no accompanying fever, pain, distension, air hunger, or altered blood pressure, although the patient's appearance was one of anxiety The drain was shortened, and a profuse outpouring of bile promptly resulted, which continued for several days and then gradually decreased, while the patient appeared progressively better Biliary drainage had ceased at the time of dismissal, 15 days postoperative Biliary leakage in this case undoubtedly occurred through the incision in the common duct

Case 5—A female, age 27, was admitted to the University Hospital, 16 days after a cholecystectomy, performed in another institution The common duct had not been explored and the abdomen was closed without drainage Four days after operation severe upper abdominal pain radiating to the shoulders, fever, and distension had developed and increased, accompanied by nausea and vomiting No evidence of shock had appeared On admission, the clinical and roentgenologic findings were typical of a large right subdiaphragmatic collection of fluid, and 700 cc of clear bile were obtained on surgical drainage Convalescence was stormy but the drainage gradually lessened, and complete recovery followed In this case it was impossible to demonstrate the site of the biliary perforation

Case 6—A female, age 68, was admitted to the University Hospital, 48 hours after the onset of severe upper abdominal pain, distension, and collapse When first seen, the patient was *in extremis*, with marked cyanosis, and pronounced shock A diagnosis of coronary thrombosis was made The patient expired two hours after hospitalization Postmortem examination disclosed 1,000 cc of free bile in the peritoneal cavity, a gangrenous gallbladder and stones both in this structure and in the common duct Careful study of the entire biliary tract disclosed no obvious site of perforation *Pathologic Diagnoses* Bile peritonitis, gangrenous cholecystitis, and paralytic ileus

Case 7—A female, age 60, was admitted to the University Hospital, with a history of eight years of chronic calculous cholecystitis, with one occurrence of jaundice The patient was extremely obese, with a marked hypertension Cholecystectomy with drainage, carried out under spinal anesthesia, revealed a hydrops of the gallbladder and a stone impacted in the cystic duct The common duct appeared normal and was not explored The patient went into shock on the table, and remained so for 24 hours The temperature, pulse, and respirations then began to mount, with attendant signs of cardiac failure Profuse drainage of bile was noted escaping along the abdominal drain, which continued until the patient expired 48 hours postoperative Postmortem examination disclosed 200 cc of bile in the right subdiaphragmatic space and right colic sulcus A definite perforation of the cystic duct stump, proximal to the site of ligation, was found The common duct was dilated but no stones were demonstrable *Pathologic Diagnoses* Perforation of cystic duct stump, bile peritonitis, pulmonary edema, and atelectasis

Case 8—A female, age 60, was admitted to the University Hospital, with a history of long standing chronic calculous cholecystitis, with intermittent common duct obstruction. Cholecystectomy and choledochostomy were performed, and stones were found in both the gallbladder and common duct. Recovery was uneventful, and a cholecystogram taken on the twelfth postoperative day, before removal of the T-tube, showed the common duct patent and well visualized. The patient was dismissed on the sixteenth postoperative day.

Twelve days later she was readmitted with a history of two days of severe epigastric pain, gradually moving to the lower abdomen. Examination showed the patient to be acutely ill, with severe crampy abdominal pain, marked distension, definite clinical jaundice, and clay-colored stools. Vomiting was not a feature. Temperature 102° F, pulse 120. Exploration revealed a diffuse bile peritonitis but demonstrated no definite site of perforation. Drains were introduced down to the region of the common duct. The patient expired 48 hours postoperative. *Postmortem*: Diffuse bile peritonitis, stone impacted in ampulla of Vater, moderate dilatation of common duct, perforation of stump of cystic duct, partial intestinal obstruction, and bronchopneumonia.

Etiology—Bile has a strong natural tendency after its formation in the liver to follow its natural course down through the hepatic and common ducts and pass into the duodenum, provided there is no obstruction at the sphincter of Oddi. This same tendency continues even though an abnormal opening may occur in the duct wall above the sphincter.

Cope¹ has suggested as three factors which normally tend to prevent any extensive extravasation of bile: (1) The low pressure of biliary secretion and possibly its intermittency, (2) the natural tendency to closure of any abnormal opening, and (3) the readiness with which nature closes an opening in the extrahepatic ducts, even more striking than with other muscular tubes in the body.

A review of the subject of biliary peritonitis, however, discloses a variety of ways in which this condition may be produced:

- (1) Biliary peritonitis without gross evidence of perforation
 - (a) Idiopathic leakage
 - (b) Microscopic perforation
 - 1 Through gallbladder
 - 2 Through extrahepatic ducts
 - 3 Through intrahepatic ducts, with capsular rupture
- (2) Bile peritonitis following trauma
 - (a) Trauma to the abdomen
 - 1 Rupture of the common duct
 - 2 Rupture of the gallbladder
 - 3 Rupture of the liver
 - (b) Leakage from the gallbladder bed following cholecystectomy
 - (c) Absorption or slipping of a cystic duct ligature
 - (d) Increased pressure in the biliary tree following cholecystectomy from overlooked common duct stone
 - 1 Ruptured stump of cystic duct
 - 2 Ruptured common duct
 - 3 Rupture of intrahepatic duct

- (3) Bile peritonitis resulting from infection
 - (a) Perforation of the gallbladder
 - (b) Perforation of common duct
 - (c) Perforation of subserous duct in liver
- (4) Bile peritonitis secondary to increased intraductal pressure and perforation from unusual causes
 - (a) Stricture of duct
 - (b) New growth occluding ducts
 - (c) Congenital cystic dilatation of common duct

A large number of cases of bile peritonitis without demonstrable perforation of the biliary tract have been reported in the continental literature during the past 40 years. Filtration of bile through the walls of the gallbladder or extrahepatic ducts was suggested as a route of spread, as was filtration through channels of Luschka's glands. Careful study of these cases, however, began to show that a small perforation, often microscopic in size, could be demonstrated in the majority of instances. These perforations often could only be identified by serial section at the site, because of their small size they would leak only when the intraductal pressure was increased, but would be quickly covered over as the pressure was relieved. A ruptured subserous bile duct on the liver surface was found to be one of the most frequent sites for these microscopic perforations. Schlaepfer,² after collecting 15 instances of this type from the literature, concluded that almost invariably a chronic cholangitis was present, with the perforation resulting from a sudden increase in intra-abdominal pressure. Cope¹ reported six personal cases of diffuse bile peritonitis without obvious perforation, and concluded that the most logical explanation was a small localized infection or ulceration in the mucosa of the biliary tree, with resultant microscopic perforation. Pohlman³ stated that experimental work does not establish the existence of true biliary peritonitis in man without demonstrable perforation, although the perforation may be very difficult to find.

Bile peritonitis from a traumatic rupture of the gallbladder or common duct has been reported but is rare in the absence of preexisting disease in these structures. Traumatic rupture of the liver permits the escape of some bile but this feature is usually greatly overshadowed by the associated hemorrhage.

The presence of accessory hepatic ducts entering the gallbladder directly from the liver bed has often been observed. Mentzer⁴ found these accessory hepatic ducts present in eight of 96 consecutive autopsies. They may easily be confused with collapsed veins during the performance of a cholecystectomy under ether anesthesia, which reduces the flow of bile. Probably these accessory hepatic ducts often account for the leakage of varying amounts of bile following cholecystectomy. Fear of such biliary leakage has been the principal reason for adherence to the principle of instituting drainage following all types of biliary surgery. Saunders,⁵ Abell and Abell,⁶ Wolfe,⁷ and Graham,⁸ have all reported series of cholecystectomies closed without drainage,

with gratifying results. None reported any fatalities from bile peritonitis, although Graham observed two instances of bile leakage after cholecystectomy, with subsequent recovery. Many other experienced surgeons feel that accessory hepatic ducts are a real hazard following cholecystectomy and insist upon routine drainage.

Diffuse extravasation of bile, resultant from premature absorption or slipping of the cystic duct ligature following cholecystectomy, undoubtedly occurs. If drainage has provided an avenue of escape for the bile, recovery may result without interference. Wolfer has demonstrated that a ligated cystic duct undergoes necrosis at the site of ligation, and closure of the duct end is dependent upon a proliferation of the adjacent tissue. These facts would suggest the advisability of covering over the ligated cystic duct stump with the adjacent peritoneum and not permitting the end of the drain to be in immediate contact with this site.

Overlooked common duct stones, with subsequent increased pressure in the biliary tree following cholecystectomy, may be followed by bile peritonitis, resultant from perforation of the biliary tree. The site of perforation may be through the ligated stump of the cystic duct, through the common duct, especially if this structure was opened at operation, or through a dilated intrahepatic bile radical on the hepatic surface. Wolfson and Levine⁹ reported three cases of diffuse bile peritonitis developing between the thirty-fifth and forty-second days after cholecystectomy and choledochostomy. Two of these patients recovered following drainage of the common duct area while the third, at autopsy, showed a definite perforation at the site of the previous common duct incision with several stones in the lower portion of this duct. These authors attributed perforation to a localized infectious process in the wall of the common duct at the previous operative site.

Infection, whether acting alone or associated with external or surgical trauma, undoubtedly plays a major rôle in many cases of bile peritonitis. The association of cholangitis and hepatitis with cholecystitis is now a well-established and accepted fact. Smith¹⁰ has reviewed 12 fatal cases of bile peritonitis from ruptured intrahepatic ducts. All these patients, 80 per cent female, were in the latter half of life, and all gave a long history of typical biliary colic, with intermittent common duct obstruction. In each instance, it was concluded that a chronic inflammatory process associated with gallstones had existed in the biliary channels for years. An exacerbation of the inflammatory process affected a group of the bile ducts in a small scar beneath the liver surface, with resultant necrosis of the overlying tissue, rupture, and peritonitis. Schlaepfer² came to similar conclusions in a study of his cases of intrahepatic rupture.

Perforation of the inflamed gallbladder very rarely results in the production of diffuse bile peritonitis. One of our seven cases developed incident to a gangrenous gallbladder, with associated common duct stones, but no definite site of perforation was demonstrable at autopsy. Several years ago, the author, with E. L. Eliason,¹¹ found, in a review of this subject, that while the incidence of perforation of the gallbladder varied from one to three per

cent in the reported series of biliary admissions, few of these cases showed evidence of biliary peritonitis. In a series of 490 consecutive biliary admissions, perforation of the gallbladder had occurred in nine cases, but diffuse bile peritonitis was not found in a single instance, undoubtedly due to the fact that the perforating gallbladder tends to be well walled-off by adjacent structures before actual perforation occurs.

That strictures and new growths occluding the biliary ducts may contribute to perforation and biliary peritonitis is quite evident. These conditions readily produce the element of obstruction and, with associated infection, set the stage for perforation. Caulfield¹² reported two cases of bile peritonitis occurring in infants during the first month of life, with one recovery. In the fatal case, a stricture of the lower common duct was found and the bile escaping through a perforation above this was localized in a serous lined sac in the upper abdomen. It was suggested that this picture might represent the first stage of the so-called idiopathic dilatation of the common duct seen in older children.

Our observations lead us to believe that increased pressure within the biliary tree from overlooked common duct stones is the most frequent basic factor in the production of biliary peritonitis. The presence of such stones in three of our five fatal cases supports this conclusion.

Pathology—The seriousness of an extensive extravasation of free bile within the peritoneal cavity has been the subject of a great deal of controversy. Some insist that free, uncontaminated bile within the peritoneal cavity is never lethal, and others consider death inevitable if sufficient bile escapes and is not drained. The considerable number of fatal cases following perforation of the biliary tree would seem to refute the statement that bile peritonitis is never fatal, and yet patients are observed who, for long periods, have harbored extensive intraperitoneal collections of bile without being seriously ill.

It is very important to differentiate accurately between bile peritonitis and ascites, since these conditions may be confused. Ravdin, *et al*,¹³ have shown that true biliary peritonitis demands the presence of free bile in the peritoneal cavity with a corresponding peritoneal irritation, while biliary ascites appears in cases of common duct obstruction with portal stasis in which efforts at setting up a collateral circulation are only partially adequate. In this latter condition, the resultant ascites is bile-stained from the general icterus and the bile salts present come from the blood bile salts rather than a filtration or perforation through the hepatic duct walls.

In an effort to better understand the effect of free bile within the peritoneal cavity, numerous experimental studies have been undertaken in recent years,^{14 15 16, 17 18 19 20} the majority of which have been made on dogs. Many of the published results conflict and do not correspond to clinical cases observed. Mentzer²¹ has pointed out that bile peritonitis in the dog is not comparable to that seen in man, since the bile of the dog is approximately 40 times as lethal when extravasated intraperitoneally as is human bile.

The experimental studies, published to date, suggest that free bile in the peritoneal cavity produces its serious effects through one or a combination of several of the following ways

- (1) Toxic action of one or more of the products present in bile upon tissues
- (2) Infection carried into the peritoneal cavity by the bile or subsequently developing through contamination
- (3) Production of a condition simulating surgical shock through the outpouring of large amounts of plasma-like fluid into the abdomen from the blood stream, associated hemoconcentration, lowered blood volume, and fall in blood pressure

The former concept that bile peritonitis produced death through toxic action of the bile salts and bile acids is supported by few investigators to-day. It is probable that the action of the bile salts upon the peritoneum makes this structure less resistant to infection. Mentzer,²¹ Rewbridge,²² and Weinberg and Levenson,²³ all consider that pathogenic bacteria passing through a peritoneal barrier damaged by the action of the bile salts are the primary cause of the fatal outcome in these cases. In clinical practice, it is unusual in a patient who has survived for any period of time to find bile which has not become infected. The usual organisms found are the streptococci, colon bacilli, and certain of the anaerobes.

In 1931, Ziegler and Oll¹⁷ observed that the peritoneal cavities of experimental animals with bile peritonitis at autopsy were filled to the point of distension with bile-stained fluid. Subsequently, Harkins, *et al*,^{18 19 20} Moon and Morgan,¹⁵ and Manson and Egiuton,¹⁶ published data demonstrating the presence of a secondary surgical shock syndrome in their animals with bile peritonitis. The extravasated bile, or its salts, injured the walls of the capillaries and venules, with resultant atony, increased permeability, and produced a tremendous outpouring of plasma from the blood into the peritoneal cavity. There resulted a concentration of the hemoglobin, fall in blood pressure, and clinical evidence of shock. This syndrome, sufficient alone to cause death in many instances, even if not lethal, so alters normal resistance that the subject is unable to resist bacteria or toxic factors which normally would not prove fatal.

Clinical Picture—It seems probable that this same shock-like picture seen in experimental animals occurs in variable degrees in clinical cases. Three of our cases of bile peritonitis demonstrated definite evidence of shock, and tachycardia was a striking clinical feature. Biliary peritonitis should, therefore, be suspected in any patient who has recently been operated upon for biliary disease and whose subsequent appearance suggests delayed surgical shock. One's suspicions are naturally confirmed if bile is found escaping along the abdominal drain in considerable amounts, as happened in four of our cases.

Bile peritonitis developing without previous biliary surgery is rarely diag-

nosed before an exploratory celiotomy Power²⁴ observed that early cases simulate a perforated peptic ulcer, although the picture does not seem so acute. When the patient is seen later, ruptured appendicitis, general peritonitis, pancreatitis, or intestinal obstruction may be suspected. These patients may even simulate cardiac emergencies, as one of our cases, admitted *in extremis*, was considered to be a coronary thrombosis until autopsy disclosed the true nature of the lesion. Exploration, and finding of free bile in the peritoneal cavity, make the diagnosis, although in many instances the exact site of perforation cannot be demonstrated.

Treatment—The successful treatment of bile peritonitis demands adequate drainage as soon as the condition is recognized. Ideally, the perforation should be closed in addition to abdominal drainage, but rarely is one able accurately to identify this site, since the patient's condition usually demands rapid exploration, with a minimum amount of manipulation. All free bile should be removed by suction, and the pelvis and subdiaphragmatic areas emptied as completely as possible. Drains are placed down to the region of the common duct, occasionally it is of value to drain the pelvis.

Postoperatively, every effort should be directed toward support of the patient. The large quantities of fluid lost should be replaced by parenteral routes and a transfusion is of great value. Blood plasma, if available, should replace that which has passed into the peritoneal cavity from the blood stream. Administration of adequate fluid will overcome the hemoconcentration and relieve the shock-like features of the condition.

Mortality—Diffuse biliary peritonitis is an extremely serious complication following biliary surgery, and results in a high mortality rate. Cope reported a mortality of 66 per cent in his six cases, our mortality was 62 per cent. The fulminating cases tend to expire in a very short period of time, in spite of all treatment, while infection is a major hazard in those in whom the process develops more slowly. All hope of improving the results in this series of patients would seem to lie in suspecting this complication when certain of its symptoms and signs are present, and the institution of immediate drainage.

SUMMARY AND CONCLUSIONS

(1) The problem of diffuse and localized bile peritonitis is discussed together with a presentation of eight cases.

(2) An outline of the various ways in which this complication may arise is presented together with a discussion of the resultant pathology.

(3) The mortality is high, ranging from 50 to 75 per cent in the reported clinical cases. The mortality in our series was 62 per cent.

(4) Treatment demands exploration as soon as the condition is suspected, with surgical drainage and energetic postoperative therapy.

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BLACK WIDOW SPIDER BITE

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THE EFFECT of the bite of *Latrodectus Mactans*, or Black Widow spider, is not in itself a surgical problem. However arachnidism is occasionally mistaken for an acute abdominal condition requiring immediate operation, a mistake comprehensible in view of the extreme severity of abdominal pain following Black Widow spider bites, the difficulty of obtaining an adequate history after the onset of severe symptoms, and the frequent failure of the victim to attach importance to the comparatively slight sting of the actual bite or to associate it with the excruciating abdominal cramping which begins shortly afterwards.

The Black Widow spider bite and its symptoms have been known to some extent for many years,^{2, 16} but only within the last 14 years has the frequency of the condition been recognized and reported. During this period a number of articles dealing with the subject of arachnidism have appeared in various medical periodicals but only twice have surgical journals published reports on the subject.^{37, 38} Because the Black Widow spider bite is far more frequent than was formerly supposed and because its symptoms simulate an acute abdominal condition, the following discussion is offered.

In the series of 24 cases herewith tabulated, 15 were collected from the records of Vanderbilt Hospital, Nashville, Tenn., from 1925 to 1939, and nine cases were seen by the writer during five years of private practice from 1935 to 1940. An examination of the case reports will reveal the following salient facts:

No cases were reported prior to 1933, and since that time the number seen and reported each year are as follows:

1933-1, 1934-1, 1935-2, 1936-4, 1937-7, 1938-5, 1939-1, 1940-3

In 14 of the 24 cases the Black Widow itself was actually seen. In the other ten cases the history and subsequent course of symptoms leave no doubt that they were clear and authentic cases of Black Widow spider bites.

The location of the bites is of interest. Eleven were bitten on the penis, four on the buttocks, one on the scrotum, one on the thigh, four on the arms and hands, one on the chest, one on the knee, and in one case the site was not mentioned. Sixteen of the victims were bitten while in a privy, two inside a house, two on a porch, and only four out of doors.

The bites occurred during the hours of darkness in 13 cases, during the daytime in nine cases and no mention is made of the time in the other two cases.

There is no significance in age-grouping, there being one patient 14 months old, and one 78 years old, with a scattering of different ages between the two.

It is interesting to note that 22 of the cases were males, there being only two females bitten

The onset of symptoms varied from five minutes to two and one-half hours following the bite. In the majority of the cases severe pain was felt within 30 minutes. As a rule, pain continued for a considerable period of time. The time of disappearance of pain was reported in 20 cases, the duration of time varying from one to three days. The average duration of pain was 24 hours.

The time of year seems to be closely related to the number of cases seen. In this series of cases the season extends from April through October. The following are the figures for the number bitten each month:

April-2, May-3, June-5, July-1, August-5, Sept-3, October-5

One patient was bitten twice, both times on the penis while in an outdoor privy. There was an interval of 41 days between the two bites. The symptoms following the second bite were less severe than those which succeeded the first. This fact is probably attributable to the amount of venom injected rather than to an acquired immunity as, according to D'Amour, immunity is acquired slowly and after repeated injections of the venom.

In the series reviewed, one fatality occurred, and one case in which mistaken diagnosis led to celiotomy. Both of these cases are herewith reported.

Case 1—Fatality Hosp No 15034 W D, white, male, age 69, was admitted to Vanderbilt Hospital at 1 00 P M, June 28, 1937. He had been treated in the Out-Patient Clinic intermittently since June, 1935, for hypertension, arteriosclerosis, duodenal ulcer, and arthritis of the lumbar spine. He had been feeling quite well until seven and one-half hours before admission. At that time he had been bitten on the scrotum by a "small black spider" while he was sitting in a privy. About 15 minutes after having been bitten he had a stinging sensation on the scrotum which was followed by severe deep pains in the upper thighs. The pain spread downward to the knees and up into the abdomen to the level of the umbilicus. He consulted a physician and one-half hour before admission to the hospital was given gr 1/16 dilaudid, and gr 1/150 atropine.

Examination revealed a fairly obese, elderly man, lying rather quietly in bed, complaining of pain in the lower abdomen, genitalia, lower back and upper thighs. The important physical findings were tortuosity of the retinal vessels, thickening and tortuosity of the peripheral arteries, blood pressure 194/86, and a small red pinpoint area on the scrotum, presumably where the bite had occurred. The abdomen was only moderately rigid, with some tenderness in the lower quadrants. R B C 4,680,000, W B C 10,000, hemoglobin 14 gm, differential count normal. Pulse 80, temperature normal.

Shortly after admission the patient was given 10 cc of 10 per cent solution calcium gluconate intravenously, without appreciable relief being afforded. The only relief obtained was from hot baths, and this was temporary. At 7 00 P M 2 cc of 50 per cent magnesium sulphate was given intramuscularly. At 8 00 P M 1/6 gr morphine was given. At 9 30 P M 20 cc of calcium gluconate was administered intravenously and 1/4 gr morphine was given at the same time. At 11 00 P M 2 cc of 50 per cent magnesium sulphate was given intravenously and 1/4 gr morphine given subcutaneously. All this medication afforded very little relief. The patient became cyanotic and, in spite of the administering of caffeine sodium benzoate and adrenalin, he died at 1 40 A M the following morning. At no time was there any indication of cardiac enlargement or pulmonary edema. An autopsy was not granted.

The following is a brief case report of a patient upon whom a celiotomy was performed following a mistaken diagnosis.

TABLE I

BLACK WIDOW SPIDER BITES

Age	Sex	Location of Bite	Place Where Bitten	Time	Appearance of Symptoms	Symptoms and Signs	Treatment	Duration of Symptoms
8	M	Chest	House	6 50	15 minutes	Cramping in legs and abdomen	Morphine Calcium gluconate	30 hours
68	M	Penis	Privy	3 00 P M	Few minutes	Cramping in abdomen chest and back	Acetylsalicylic acid	12 hours
11	M	Knee and groin	Privy	4 00 P M	2 hours	Cramping in legs abdomen chest and back	Codine Sodium phenobarbital	24 hours
14 mos	F	Thumb	Porch	?	5 minutes	Restless and vomiting	MgSO ₄ intramuscularly	24 hours
13	M	Buttocks	Privy	8 30 P M	15 minutes	Pains in back and abdomen	MgSO ₄ intramuscularly Calcium gluconate	12 hours
16	M	Buttocks	Privy	Night	2 hours	Pains in back and chest	Atropin MgSO ₄ intramuscularly	12 hours
26	M	Hand	Out of doors	Day	Not mentioned	Pains in wrist arms shoulders and abdomen	Morphine	?
17	M	Penis	Privy	11 00 P M	1-2 hours	Generalized aching	'Pills' Calcium gluconate	?
17	M	Penis	Privy	6 45 P M	10 minutes	Cramping in abdomen aching in back	Celiotomy	24 hours
40	M	Penis	Privy	1 hour	1 hour	Cramping in abdomen back neck	Morphine	24 hours
15	M	Buttocks	Privy	?	1 hour	Pains in knees hips and chest	Dilaudid	Did
69	M	Scrotum	Privy	5 30 A M	30 minutes	Pains in thighs and abdomen	Atropin Calcium gluconate	
18	M	Buttocks	Privy	1 00 P M	Few minutes	Pains in groins back and abdomen	MgSO ₄ intravenously	12 hours
35	M	Penis	Privy	Night	Few minutes	Pains in thighs abdomen back legs shoulders and neck	MgSO ₄ intramuscularly	24 hours
15	M	Arm	Field	10 30 A M	1½ hours	Pains in arm back abdomen and thighs	Hot baths Morphine	24 hours
37	M	Penis	Privy	6 00 P M	15 minutes	Pains in lower abdomen	MgSO ₄ intramuscularly	24 hours
35	M	Penis	Privy	8 00 A M	10 minutes	Pains in thighs abdomen and back	Morphine Dilaudid	3 days
4	F	Thumb	Out of doors	5 00 P M	Few minutes	Pains in arm back abdomen and thighs	Calcium gluconate	
16	M	Thigh	Bed	3 00 P M	1½ hour	Restless and crying	Hot baths One ampoule antivenom	1 hour
37	M	Penis	Privy	6 00 P M	15 minutes	Pains in abdomen back and neck	Morphine	24 hours
66	M	Penis	Privy	8 00 P M	30 minutes	Aching in lower abdomen	MgSO ₄ intramuscularly	12 hours
78	M	Penis	Privy	9 30 P M	30 minutes	Cramping in abdomen chest and back	Morphine	3 days
21	M	Penis	Privy	8 45 P M	2½ hours	Cramping in abdomen and back	Calcium gluconate	12 hours
36	M	Penis	Privy	8 30 P M	15 minutes	Cramping in abdomen and chest	Morphine Calcium gluconate	10 hours
				9 00 P M	Approximately 1 hour	Cramping in abdomen thighs back and arms	Calcium gluconate	24 hours
						Cramping in abdomen thighs back and arms	None	Seen 14 hours after bite

Case 2—Hosp No 80568 H J, white, male, age 40, was admitted to Vanderbilt Hospital, August 28, 1936, complaining of severe abdominal pain of three hours' duration. The attack began with a cramping in the abdomen necessitating a bowel action and, after returning from the out-door privy, the pain became much worse. In an hour he was suffering severely. Because of this he came to the hospital and was admitted three hours after the onset of pain. Further questioning revealed the fact that four years previously he had had an attack of abdominal pain associated with hematemesis and was told that he had a stomach ulcer.

Examination on admission showed a middle-aged white male in severe pain, in fact, so severe that a careful history was hard to obtain. He was complaining of pain in the abdomen, back, and neck. The significant physical finding was limited to the abdomen which was board-like. The pulse and respirations were increased, temperature normal, WBC 6,900, urine negative. A roentgenogram of the abdomen, in an upright position, showed no air under the diaphragm. *Preoperative Diagnosis* Ruptured peptic ulcer. The abdomen was opened and nothing of significance was found.

The following day, when the patient was more comfortable, a careful history revealed the fact that he remembered having been bitten while in the privy and having seen a black spider. He did not think of attributing his abdominal pain to this cause. His recovery following the operation was uneventful and he was discharged from the hospital after nine days.

The Spider—The Black Widow spider, or *Latrodectus Mactans*, has been found in all the states of the United States with the exception of Vermont and in Canada. It is frequently found near human habitations but also lives in woods and fields. It has a preference for protected places. In the writer's experience, specimens have been easily found in basements and out-buildings, under boards and rocks and in cans and pipes. As a rule, the spiders are not found in large numbers in old buildings where the basements and corners are filled with old webs but they are easily discovered in new, clean basements.

The Black Widow is a common spider. During the summer of 1938 the writer killed more than 20 in and around his house in Winchester, Tenn. During the summer of 1937 a neighbor found more than 80 spiders in his house or adjacent out-buildings. D'Amour and his associates¹⁸ collected 6,500 specimens in the course of one summer while studying the effects of Black Widow venom. In a letter received recently from Sharp and Dohme, of Philadelphia, in reply to an inquiry regarding the manufacture of antivenin *Latrodectus Mactans* the following statement was made: "We have experienced no difficulty in obtaining Black Widow spiders. During the summer months they occur abundantly in low lying fields on the coastal plains of the Middle Atlantic States."

In view of the tremendous number and wide distribution of these spiders it would seem that surprisingly few persons are bitten. The explanation is apparent if the actions of the spider are observed. When the web of a Black Widow is disturbed she retreats with rapidity and even when cornered she seldom makes a show of resistance or offers to bite. Ordinarily, a human being is bitten only when the spider is crushed against the body or when the web is disturbed in the dark or under some other condition which causes the spider to mistake the disturbing object for its usual prey. Sometimes a person is bitten in bed, presumably when he mashes the spider. Occasionally

one is bitten when lifting boards or rocks. More frequently bites occur when the web is disturbed in the dark as indicated by the large number of patients bitten at night in privies when the web is agitated and the spider attacks without seeing what object has been entangled.

The Black Widow is easily identified. It is the female of the species that is poisonous and there is no other spider that is at all similar in appearance. The mature female is solid black and has a large spherical abdomen and long, strong-looking legs. On the ventral surface of the abdomen is a bright red hour-glass marking. The adult male has legs of the same type but a much smaller body. Its markings are quite different, there being white, orange and brown bands and spots on its body and contrasting light and dark bands on its legs. The smaller, immature females have a row of red dots on the dorsal surface in addition to the red hour-glass marking on the ventral side. When first hatched the male and female are identical in appearance but as moulting progresses they assume their respective characteristics.

The web of the Black Widow is easily identified. It has no regular pattern. Its threads are coarse and irregularly spaced. There is no well-developed funnel hiding area.

A complete discussion of the characteristics and life history of the Black Widow spider can be found in a publication by D'Amour and his associates,¹⁸ and also in an article by Blair.¹⁰

The Black Widow is armed with a pair of hollow fangs connected to a pair of poison glands. The latter are located in the cephalothorax just behind the eyes. Microscopically, they are composed of a basement secreting layer of cells with a surrounding layer of muscle.¹⁸ The latter structure is considered to be important and it is thought that the muscle layer is subject to the active control of the spider, the amount of venom injected being thus regulated.

Studies by D'Amour and his associates show that the average adult female spider carries venom in its poison sacs which, when dried, produces 0.064 mg of solid residue. One-fourth of this amount of venom when dissolved and injected into young rats will kill about half the number treated. The venom retains its potency when dried but deteriorates rapidly in solution. Using mortality statistics, they conclude that, weight for weight, Black Widow venom is 15 times as toxic as the venom of the rattlesnake.

Symptoms and Treatment of Black Widow Bites—The course of symptoms following the bite of a Black Widow spider is striking. Usually the victim is in extreme pain when first seen, and is unable to remain still long enough to be examined properly. The greatest pain is centered in the abdomen with some involvement in the back, hips and lower chest. The pain usually begins in the muscle groups nearest the site of the bite and spreads toward the abdomen. If the bite is on the hand, the forearm, upper arm, shoulder, chest and abdomen are successively involved. If the bite is on the genitalia as is frequently the case, the pain is in the hips and thighs first, spreading later to the back, abdomen and lower chest.

In a typical case the patient gives a history of having felt a bite or sting,

like the sting of a wasp or the prick of a splinter. The bite may be ignored and recalled only when the patient is questioned directly. Usually within 30 minutes, sometimes after a longer period, the victim begins to have a dull cramping in the muscle group nearest the site of the bite. By the time the pain has spread into the abdomen, back and lower chest, it is very severe and equals or exceeds that of ruptured peptic ulcer, kidney colic, acute appendicitis or coronary occlusion.

Examination reveals obvious pain. The abdomen is board-like but moves with respiration. Later, pulse and respirations are somewhat increased. Temperature is usually normal during the first few hours but may become slightly elevated later. There may be nausea or vomiting but these symptoms do not necessarily appear.

The bite usually produces no local signs or symptoms but sometimes the fang marks can be seen—small red dots and, in delicate tissues such as the penis, a very small area of local edema is seen.

The various laboratory procedures do not aid materially in the diagnosis. There is apt to be a moderate leukocytosis but this is not constant. The red blood count, hemoglobin, differential and urine examination show no significant changes. The spinal fluid pressure may be elevated but is normal as to cellular elements.

Morphine is usually given. It affords little relief and is usually repeated. Other types of treatment are described below. After several hours the pain is somewhat abated but may recur in milder character for as long as two or three days.

Because of the severity of the pain it is sometimes difficult to obtain a satisfactory history. If the possibility of spider bite is not considered, a mistaken diagnosis of an acute abdominal condition may be made.

A great many types of treatment have been suggested for relieving the symptoms of Black Widow spider bites. Of these none offers consistent relief. Morphine and the opium derivatives help only to a small extent. The barbiturates are not effective. Magnesium sulphate given intravenously in 10 per cent solution and intramuscularly in 25 per cent solution is said to be of considerable benefit. Calcium gluconate given intravenously in dosages of 10 cc of 10 per cent solution is effective to some extent in relieving pain. Lumbar puncture has been suggested as a method of affording some relief. In certain cases hot baths give a great deal of additional relief.

Serum therapy is in the experimental stage. Serum from patients who have been bitten has been used but it is of doubtful efficacy. D'Amour¹⁸ found that in rats a serum could be made which, in one cubic centimeter doses, would protect them against four times the average lethal dose of spider venom. This immunity was built up quite slowly, and in rats 27 injections of venom were given over a period of ten weeks in order to produce a potent serum. There is a serum available commercially which is said to neutralize the venom from 750 spiders. This was used in treating one of the last two cases seen by the writer, the victim being, in this instance, a four-year-old

girl The child was playing in the yard with a tin can in which there was a spider She was bitten on the hand and in a few minutes began to complain One hour after the bite she was seen in the hospital She was in great pain and unable to lie quietly On the thumb was a small reddish area which was said to be the site of the bite The abdomen was rigid, the temperature normal, and the pulse elevated The child's mother stated that the spider was black with a red spot on its abdomen A single dose of the antivenin was given subcutaneously No other medication was given In an hour the patient was asleep and the abdomen soft She was kept in the hospital two days for observation and there was no recurrence of pain It will be interesting to note whether similar results are obtained by the use of this antivenin in the future

End-Results—Fatalities following Black Widow spider bites are quite uncommon notwithstanding reports by Bogen,¹⁴ who collected approximately 600 cases of such bites with 40 recorded deaths This would indicate a mortality rate of 6.6 per cent The records of these deaths were not obtained from published articles but were collected from death certificates, newspaper reports and personal communications

In 248 cases, collected from the literature (references 6, 9, 14, 16, 17, 20, 23, 24, 27, 28, 29, 33, 37, 39, 40, 41, 42, 44, 48, 50, 51, 55, 56) there were no recorded fatalities Among them was Ginsberg who, in reporting 96 cases, remarked that none died and that none of them was seriously ill

Although there have been deaths resulting from Black Widow spider bites, a review of the literature fails to reveal any deaths reported in detail

Judging from the cases reviewed in the present series, it appears that arachnidism usually results in complete recovery without sequelae after a period of three days or less

SUMMARY

(1) Twenty-four cases of Black Widow spider bites are analyzed as to age, sex, location of bite, place when bitten, appearance of symptoms, treatment, and duration of symptoms

(2) Two cases are reported in detail, one being the only fatality occurring in the series and the other, a case in which mistaken diagnosis led to celiotomy

(3) The spider, his distribution, habits and venom are discussed

(4) The symptoms and treatment of Black Widow bites are discussed

(5) End-results of Black Widow bites are discussed

CONCLUSIONS

(1) The bite of *Latrodectus Mactans*, or Black Widow spider, is more common than was formerly supposed

(2) Symptoms of Black Widow bite may simulate an acute surgical condition

(3) Fatality resulting from the Black Widow spider bite is rare

(4) No uniformly satisfactory treatment for the relief of symptoms has been found

(5) The single case in which antivenin was used, and resulted in immediate relief, suggests the possibility that its further use may afford more adequate relief than has heretofore been obtained by other methods of treatment

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SEBACEOUS GLAND CARCINOMA

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THIS PAPER is a discussion of an interesting malignant tumor of sebaceous gland origin, with a case report of such a tumor that arose in the fifth toe of the right foot. We feel that the location, the somewhat unusual type of tumor, and the problem arising in the choice of treatment are worthy of reporting.

Since the type of therapy for tumors depends upon their histology, the pathologic diagnosis should be accurately determined. Tumors that may metastasize demand some variations in treatment from those which do not. There are two divergent opinions regarding sebaceous gland tumors. Stout,¹ Darier,² and LaCassagne,³ feel that these tumors resemble and behave like nonmetastasizing basal cell epitheliomata. Darier, and Favie, *et al*⁴ assume that the lipid material in these tumors is a degenerative change in the tumor cells. Stout is in favor of the view that the sebaceous epithelioma is simply a specialized form of the basal cell group of tumors in which there is some tendency for the cells to reproduce sebaceous epithelium. On the other hand, Hagedoorn,⁵ and Pages *et al*⁶ believe that they are malignant tumors of sebaceous gland origin and may metastasize.

About the middle of the last century, Malherbe and Robin⁷ first recognized cancers coming from sebaceous glands, however, the first reported case of which we find a complete record was that of Allaire,⁸ in 1891. In 1922, Menetrier and Ischwall⁹ reported two similar tumors occurring on the ala of the nose and on the chin in a man, age 50. In a discussion of this paper, Darier said they were only basal cell epitheliomata. Masson and Geiy,¹⁰ in 1922, reported four sebaceous epitheliomata, one of the forehead, one of the ala of the nose, and two of the scalp. These authors are of the opinion that many basal cell tumors come from sebaceous glands and in most instances display regressive metaplasia and lose their sebaceous characteristics. When they retain these lipid elements they are considered true sebaceous epitheliomata. Masson expresses the belief that any epidermal cell is totipotential and may give rise to a sebaceous epithelioma, so that it is not necessary to have sebaceous glands in a region from which a sebaceous epithelioma arises. In 1924, Gynfelte¹¹ reported an ulcerated tumor of the ala of the nose. It was his opinion, however, that this tumor was a basal cell epithelioma containing areas of the sebaceous type. While it is generally accepted that the average basal cell tumor does not metastasize, nevertheless it must be borne in mind that such tumors can, but rarely do, metastasize. We are able to accept as proven examples the cases reported by Beadles¹² (one case), Finneid¹³ (two cases), and Mulzer¹⁴ (two cases). Forty cases of sebaceous epithelioma of the eyelids were collected in 1926 by Moirax,¹⁵ no details were given. He added one case of his own. Hagedoorn,⁵ in 1934, collected 59 cases of sebaceous epitheliomata of the eyelid, and also added another case to the literature.

Metastasis occurred in the cervical nodes in his patient four years after surgical treatment of the primary tumor. We assume that Morax's cases are included in Hagedoorn's collection. Prior to 1934 eight sebaceous gland carcinomata were reported, by five authors in locations other than the eyelids. Since this contribution in 1934 14 additional cases have been recorded by various authors.

Soudille⁸ in 1894 was the first author to report metastasis. This occurred in the preauricular lymph nodes. He also was the first to report local recurrence which followed operation upon an upper eyelid tumor.

Allaire,⁸ in 1891 was the first to use surgery on a sebaceous gland cancer. Without knowledge of the details of Morax's cases we credit Hughes¹⁶ as the first to use radium therapy, which he tried in 1932, following five unsuccessful operations. Hagedoorn¹⁷ in 1937 used radium as initial therapy; this was followed in nine months by surgery for the recurrence. In 1938 Pages *et al*⁶ first reported the use of roentgenotherapy. It was directed to the metastasis and postoperative local recurrence of the eyelid growth, with apparent success.

While not conducting an exhaustive review of the literature we have, however, obtained the following information from available sources. Most of the patients were males over fifty years of age, with involvement of the eyelid, principally the upper lid. Other locations include ala of the nose, scalp, forehead, ear, chin, mammary region, scapular region, eyebrow, and scrotum. For the most part the tumors were of slow growth. The treatment in the majority of the cases was excision. Recurrence after treatment of the primary tumor was noted 34 times in 18 cases. In the literature there is mention of metastases having occurred five times in 40 cases.

Case Report—A white male, age 60, was first examined October 5, 1939. He gave a history of a gradual enlargement of the right fifth toe that was first noticed two years previously. From time to time the toe suffered slight trauma. The first evidence of more rapid enlargement was noticed in May, 1939, this occurred after an injury more severe than usual. While not painful the toe eventually became uncomfortable because of pressure from his shoe. There was no recent loss in weight. F.H. There was no evidence of cancer, tuberculosis or diabetes. P.H. There was no history of acute or chronic disease since childhood.

Physical Examination—The local examination showed a hard, smooth, partially encapsulated tumor of the fifth toe, right (Fig. 1), measuring 4×3×3 cm. Palpation failed to demonstrate definite connection with either phalanx. Firmly adherent skin on the plantar surface was faintly blue, elsewhere the color appeared normal. On the medial part of the plantar surface was a small superficial lesion that suggested a mild fungus infection.

Several freely movable, shotty inguinal lymph nodes were found in each groin. In the inferior portion of Scarpa's triangle on the right side, was a hard, somewhat movable node measuring 1.5×1 cm. Roentgenologic examination showed a soft tissue tumor of the right fifth toe. In the central portion there were foci of calcification, no bone involvement was seen (Fig. 2). **Clinical Diagnoses Considered**—(1) Giant cell tumor of tendon sheath origin. (2) Fibrosarcoma. (3) Lymphangioma.

Treatment—Dr. Asa Beach. The tumor of the toe was enucleated October 7, 1939, and after histopathologic study a subsequent operation was performed October 10, 1939.

This consisted of disarticulation at the metatarsophalangeal joint. Wound healing was normal.

Pathologic Examination—Gross Dr A. O. Severance. The specimen (Fig 3) is a tumor mass measuring 4.3 x 3.2 x 2.5 cm. It is covered on all but one surface by thick skin. The portion of tumor not covered by skin is a pinkish-gray, mottled with small yellow areas. A tendon attachment, one centimeter in length, enters the tumor in this region. The cut surface of the tumor has a creamy-gray appearance, with a diffuse distribution of small yellow areas. Deposits of calcium and zones of dense tissue are encountered although most of the tumor is soft.

Microscopic—Eight sections taken from different parts of a slice through the center and from the region of incision are essentially similar. The tumor cells are arranged in fairly large, solid masses, small cords, clusters, and in a few instances in true acini (Fig 4). The supporting stroma is dense fibrous connective tissue in which are seen areas of granular degeneration of the collagen, slight round cell infiltration, and foci of calcification. Tumor cells are seen in lymphatics and in one slide, prepared by Masson's trichrome method, a blood vessel is filled with tumor cells. Some parts of the tumor show central degeneration. In some of the larger masses a central grouping of large, pale cells is seen (Fig 5). The tumor extends to the line of incision in one section, and actually invades a tendon. It does not invade the skin.

The individual tumor cells vary moderately in size and shape, have finely granular eosinophilic cytoplasm, and round to oval nuclei, with a slight to moderate amount of uniformly distributed chromatin and occasionally small nucleoli. Some of the cells are typical foam cells with light neutrophilic cytoplasm. In the sudan III preparation these cells contain many droplets of lipid and stain bright orange. Many of the other eosinophilic granular tumor cells also contain lipid as shown in this fat stain. Even cells in mitosis contain lipid material in their cytoplasm. Mitotic figures are abundant, varying from none to five per high power field and averaging two. In a few of the masses there is a slight tendency to show palisading of cells perpendicular to the basement membrane. In the stroma there is a moderate infiltration of lymphocytes. Sections taken through the wound of the toe following amputation, do not show persistent tumor cells. *Pathologic Diagnosis* Sebaceous gland carcinoma. (The essential pathologic features of this tumor have been studied and the diagnosis confirmed by Drs A. P. Stout, of New York, and Shields Warren, of Boston.)

Postoperative Course—In view of the pathologic diagnosis the patient was observed and examined every two weeks with particular attention to the right inguinal lymph nodes. For a period of four months there was no noticeable increase in size, however, on April 15, 1940, six months following amputation for the first time, a definite measurable increase in size of the hard node, measuring 2.5 x 2 cm, was demonstrated.

A consultant concurred in the opinion that a radical inguinal adenectomy was advisable, and on April 27, 1940, a solid block dissection of the right groin was performed, from above downward. The only postoperative complication was prolonged drainage of lymph from the upper part of the wound.

Pathologic Examination—Gross The tissue from the right groin is a fairly large triangular-shaped mass of fat measuring 13.5 x 11.5 cm (Fig 6). From this, 16 lymph nodes were isolated, varying from 3 to 20 mm in diameter. The largest node shows small satellite nodules of tumor extending out through its capsule.

Microscopic—Seven of the 16 nodes contain tumor. In general, the metastases resemble the primary tumor. The tumor in the nodes is less differentiated, contains more mitotic figures per high power field on an average, and contains less lipid material in fewer tumor cells as shown by the scharlach R stain. Some of these lipid-containing tumor cells are in mitosis. Three of the nodes are completely replaced by tumor and dense fibrous stroma.

Postoperative Therapy—The use of roentgenotherapy, for possible tumor extension

SEBACEOUS GLAND CARCINOMA

FIG 1

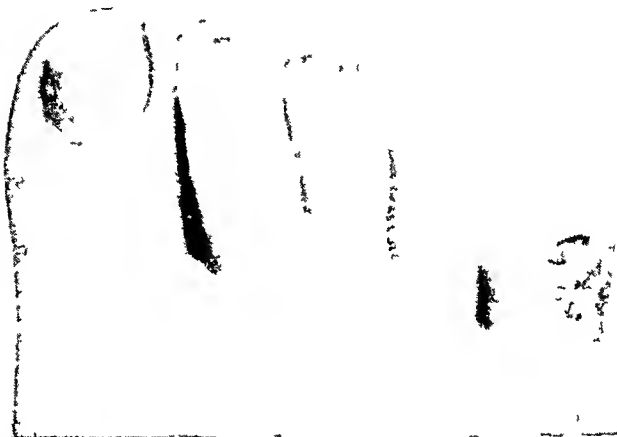


FIG 2

FIG 1—Photograph of tumor of fifth toe before operation
FIG 2—Anteroposterior and lateral roentgenograms of toe tumor
showing faint shadows of calcareous deposits



FIG 3—Photograph of tumor, in cross section, after removal

TABLE I
SUMMARY OF CASES APPEARING IN THE LITERATURE*

Author	Date	Sex	Age	Location	Duration	Treatment	Observation Notes and Results
Allaire ⁸	1891	F	11	Eyelid		Surgery	Recurrence 12 days after curettage
Sourdille ⁸	1894	M	59	U eyelid		Curettage	to preauricular lymph nodes Rapid growth Metastasis
Gross ⁸	1896	M	63	U eyelid	1 yr	Surgery 2 times	Recurrence 3 mos postoperative
Scalinci ⁸	1908	F	56	U eyelid	1 yr	Surgery	Good results
Snell ¹⁸		F	63	U eyelid	10 yrs	Excision (1905) Exenteration (1906)	Recurrence with metastasis even after eventeration
Grignolo ¹⁹	1909			U eyelid		Surgery	Invasion of orbit
Grignolo ¹⁹	1909			L eyelid		Surgery	
Menetrier and Durand ⁹	1920	F	54	Nasal ala	Few yrs	Exenteration with lymph node excision	Metastasis to preauricular lymph nodes Recurrence 6 mos postoperative Died of tumor
Cavara ¹	1920	M	67	U eyelid	Few mos		
Menetrier and Ischwall ⁹	1922	M	50	Chin and ala			
Masson and Gery ¹⁰	1922	M	63	Forehead		Surgery	Postoperative recurrence
Masson and Gery ¹⁰	1922	M	50	Scalp			
Masson and Gery ¹⁰	1922	M	79	Nasal ala			
Masson and Gery ¹⁰	1922	M	72	Scalp			
Bazy ¹⁰	1922	M		Scrotum		Surgery	Postoperative recurrence
Riva ¹⁰	1922	F	63	U eyelid	10 mos	Surgery	No recurrence
Letulle ³	1923	M	75	L eyelid	13 yrs	Surgery 2 times	Recurrence 3 yrs after first operation No metastasis No recurrence 1 yr postoperative
Michael ¹	1924	M	67	U eyelid	1 yr	Surgery 2 times	No metastasis
Grynfeldt ¹¹	1924	M	50	Nasal ala	20 yrs		Recurrence 10 yrs after first operation (1914) was excised
Morav ¹⁵	1926	M	74	U eyelid	14 yrs		
Morav ¹⁵	1926	M					Forty cases mentioned in lit
Shoje ¹	1929	F	69	L eyelid	5 yrs	Surgery	Invasion of orbit
Lazarescu and Ionescu ⁸	1930	M	67	U eyelid	2 yrs	Surgery 3 times	Two postoperative recurrences
Chailous and Kalt ⁷	1931	M	48	U eyelid		Surgery 3 times	Well 2 mos after last operation
Nastri ⁸	1931	F	57	U eyelid	5 yrs	Surgery 4 times	Three recurrences Well 1 yr after last operation
Hughes ¹⁶	1932	M	54	U eyelid	4 yrs	Surgery 5 times	Six recurrences Alive with persistent tumor
Hagedoorn ¹⁷	1934	M	66	U eyelid	2 yrs	Surgery	Metastasis present 4 yrs after operation
Lebensohn ⁹	1935	F	43	U eyelid	1 yr	Surgery 4 times	Each operation followed by recurrence Died of tumor
Hagedoorn ¹⁷	1937	F	50	U eyelid	2 yrs	Radium 2 times	months after radiumtherapy
Hagedoorn ¹⁷	1937	M		U eyelid	3 yrs	Surgery	Recurrence 9 mos postoperative
Hagedoorn ¹⁷	1937	F		U eyelid	3 yrs	Radium first then surgery	Recurrence 9 mos after radiumtherapy
Dupont ¹⁰	1937	F	61	Eyelid	3 yrs	Surgery	Satellite tumors present
Dupont ¹⁰	1938	F		Mammary region	4 yrs	Surgery	
Pages <i>et al</i> ⁶	1938	M	33	L eyelid	3 wks	Surgery first then x-ray therapy	Metastasis present at operation Recurrence and metastasis dis
Lucien and Crehange ¹¹	1939	M	41	Ear (lobe)	2 1/2 yrs	Surgery	Tumor had invaded parotid region
Dollfus ³	1939	M	46	L eyelid	12 yrs	Surgery and radium-therapy	Lymphatic invasion microscopically No disease 6 mos later
Warren and Warv ¹³	1940	M	69	Nose	18 mos	Surgery 5 times then radium then x ray	Five recurrences after surgery and 2 after irradiation
Warren and Warv ¹³	1940	M	75	L eyelid	8 mos	Surgery 2 times	Recurrence after first operation none after second (1935)
Warren and Warv ¹³	1940	F	70	Scalp	3 wks	Surgery (1937)	No recurrence
Warren and Warv ¹³	1940	F		Scalp	6 mos	Surgery (1937)	No recurrence
Warren and Warv ¹³	1940	M	70	Eyebrow	Many yrs	Surgery (1939)	Rapid growth for 6 mos prior to operation No recurrence
Warren and Warv ¹³	1940	M	63	Scapula ¹ region (r)	Few yrs	Surgery (1939)	No follow up

* The information on the last six cases was furnished by Dr. Shields Warren and Dr. Wesley N. Warv. More detailed descriptions of these cases will be forthcoming in the paper on skin appendage tumors by these authors.

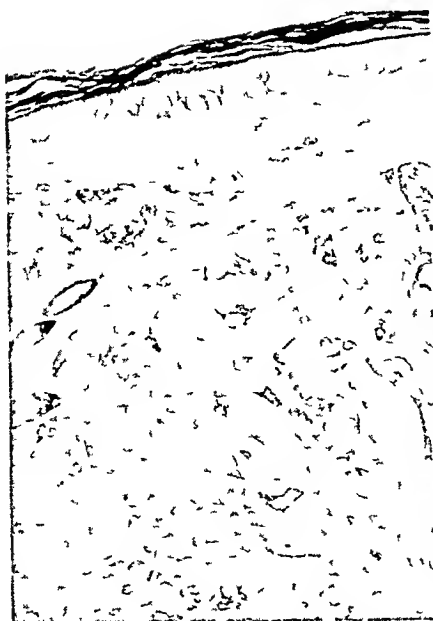


FIG 4—Photomicrograph of sebaceous gland carcinoma of toe showing relationship to epidermis and general formation of the tumor (Low power)

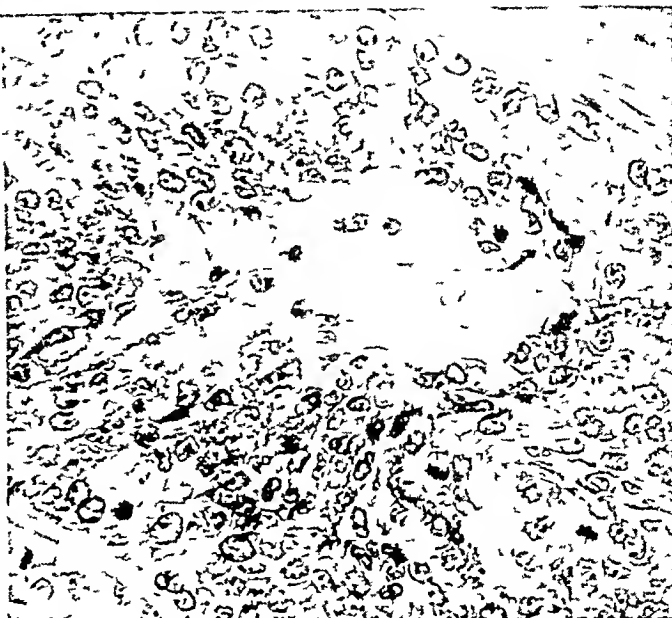


FIG 5—Photomicrograph of the tumor showing typical foam cells surrounded by the predominant type of tumor cells which contain several mitotic figures (High power)

beyond the operative site, was considered. This treatment was strongly urged by Dr A. P. Stout,¹ and it was instituted eight weeks after the groin dissection. The factors used were 200 kV, 25 ma, 50 cm, T-S-D, $\frac{1}{2}$ mm Cu plus 1 mm Al filtration. Portals varied from 10×20 cm to 15×20 cm. The pelvic and lumbar nodes were given 2,200 r each, in daily doses of 200 r. Following a month's delay 2,200 r were given to the operative site in 11 treatments.

Follow-Up—Observation over a period of 13 months does not show any evidences of persistent disease, either locally, at each operative site, or in metastases. Subsequent follow-up 24 mo after initial treatment shows no evidence of recurrence or metastasis.

COMMENT—We feel that this tumor is of sebaceous gland type, and has behaved like any malignant glandular neoplasm. In view of the controversy which this statement is likely to arouse, it is well to review the prominent features of this tumor and others of its type. Schallach R preparations show lipid material in the typical foam cells, as well as in many of the other tumor cells and even in those in active mitosis in the metastases as well as in the primary tumor. This latter is the first recorded notation, so far as we know, of this type of tumor cell containing lipid while in mitosis. Definite



FIG 6—Photograph of the deep surface of the block groin dissection showing the largest metastatic node cut in half.

acinar formation is present. Tumor cells are seen in blood and lymphatic vessels—a finding rarely, if ever, noted in basal cell epitheliomata. The dense fibrous stroma, with calcification in this tumor is not unlike that seen in the scirrhous type of breast carcinoma. A characteristic common to basal cell tumors,

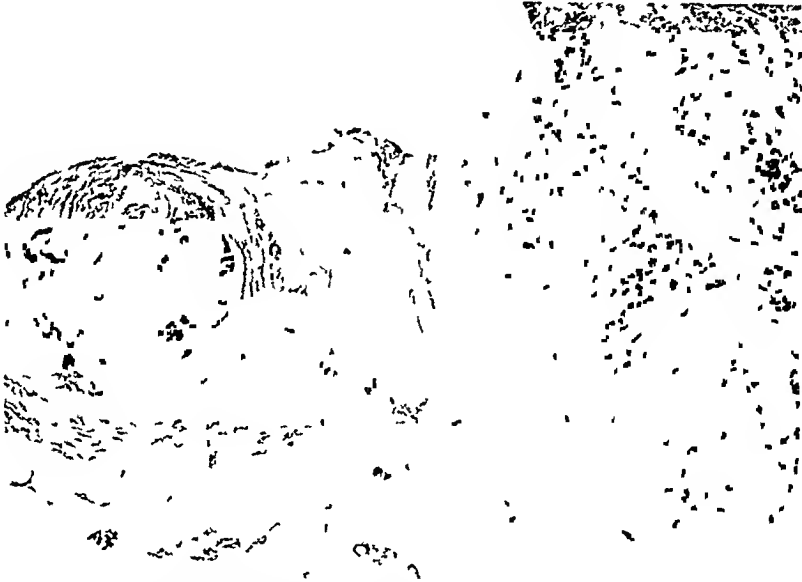


FIG. 7.—Photomicrograph showing tumor cells in an inguinal lymph node on the right and within the lumen of a tangentially cut vein on the left.

namely, skin involvement, is strikingly absent in our case. The individual tumor cells do not resemble those seen in basal cell types for they have a more acidophilic cytoplasm, have a lighter staining nucleus, and show more variation in size and shape of the cells.

The difference in clinical behavior of the sebaceous gland carcinoma and basal cell epithelioma is shown by the increased incidence of metastases in the former. We knew of six instances of metastases in 75 cases of sebaceous gland carcinomata, whereas there are only five reported metastases of basal cell epitheliomata in the literature.

In this investigation, we have assumed that the glands of Zeiss and the meibomian glands are essentially similar to sebaceous glands. Certain ophthalmologists may raise the point that these eyelid glands are not true sebaceous glands. However, they are considered specialized derivatives of sebaceous glands, and tumors arising from both types are essentially similar in appearance and behavior.

An interesting feature of this tumor is its location in an area considered devoid of sebaceous glands. We have not encountered in the literature a tumor of this type in a similar location. Another feature worthy of mention is the history of recent rapid growth, the microscopic appearance of rapid cell proliferation, and the rapid development of metastasis.

We feel that in sebaceous gland carcinoma the treatment of choice is ade-

quate surgical excision of the primary tumor, with subsequent prophylactic regional node block dissection. In instances of clinical lymph node involvement a similar procedure should be carried out. In cases in which the nodes are involved, clinically or microscopically, proper roentgenotherapy should be administered to the area of the lymph node dissection as well as to nodes which drain this region.

The prognosis in our case is poor, in spite of the treatment given and the patient's apparent well-being at this time (eight and one-half months following groin dissection).

SUMMARY AND CONCLUSIONS

(1) Forty-one cases of sebaceous gland carcinomata, with our addition, have been reviewed. This excludes Morax's 40 cases.

(2) An unusual sebaceous gland carcinoma has been discussed.

(3) The proposed treatment is adequate surgical excision of the primary tumor, regional node dissection, and roentgenotherapy when indicated.

We are greatly indebted to Dr. Arthur Purdy Stout, of the Department of Surgery, College of Physicians and Surgeons, Columbia University, New York, N. Y., for his interest, advice, and cooperation in the treatment of this patient, and in the preparation of this communication.

We greatly appreciate the aid of Dr. John Pilter Heaney, of the Department of Surgery, Presbyterian Hospital, New York, N. Y., for his assistance in the review of the literature, and to Drs. Shields Warren and Wesley N. Waiver of Boston, Mass., who have been very kind in allowing us the use of their six, as yet unpublished, cases of sebaceous gland carcinoma.

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NEUROPATHIC ARTHROPATHY OF THE ANKLE JOINT RESULTING FROM COMPLETE SEVERANCE OF THE SCIATIC NERVE

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NEUROPATHIC JOINTS develop in approximately 10 per cent of all tabetic patients. The condition was first reported by Charcot¹ (1868), and described by him as joint destruction due to abnormal stimuli, transmitted through so-called trophic nerves. In 1888, Schultze and Kahle² reported similar lesions occurring in syringomyelia, and according to Schlesinger³ the condition occurs in 30 to 40 per cent of all persons afflicted with that disease. Packard⁴ reported the first instance of a neuropathic joint developing after a peripheral nerve injury. In his patient, arthropathies of the foot and knee followed compression of the sciatic nerve by a tumor. Although syringomyelia and tabes remain the two principal causes, neuropathic joints have been reported as developing in conjunction with a wide variety of clinical conditions. For a review and classification of these the reader is referred to a recent report by Shands⁵.

There are numerous reports of neuropathic joints purported to be the result of a peripheral nerve injury^{6, 7, 8, 9}. Most of them are open to question, however, since the nature of the peripheral nerve injury is usually not clear and it is difficult to exclude the possibility of a central nervous system lesion. In fact Milgram¹⁰ doubts the existence of a neuropathic joint as the result of a peripheral nerve injury.

The following case of neuropathic joint is reported because it throws light on the pathogenesis of that condition.

Case Report—M. L., white, male, age 22, was struck in the left thigh by a red-hot rod, December 10, 1936. The resultant shock was treated in a local hospital. Three days later the patient was removed to St. Luke's Hospital and admitted to the service of Dr. W. F. Lyons.

Examination of the limb revealed that the red-hot iron had pierced the soft parts of the posterior portion of the left thigh at about the junction of the middle and lower thirds. It then had seared its way outward posteriorly, completely severing the sciatic nerve and all the hamstring muscles, but sparing the popliteal artery. The resultant soft tissue defect was approximately 15x10x4 cm. The ends of the sciatic nerve were separated by at least 6 cm. The patellar tendon reflex was active, the achilles tendon reflex absent. There was paralysis in the sensory and motor distribution of the sciatic nerve below this point.

Treatment with warm moist saline dressings was instituted and the wound responded promptly. Skin grafts were applied and by February 20, 1937, the wound was completely healed. The patient was discharged from the hospital, walking with the aid of crutches.

Knee joint stability was maintained by the intact quadriceps muscle group. The ankle joint was ataxic, anesthetic and relaxed.

Despite these handicaps, he soon learned to walk without aid. He returned to work in August, 1937. As a result of weight-bearing on, and undue traumatization of, this relaxed, paralyzed and anesthetic ankle joint, there soon developed a marked varus deformity, accompanied by a dependent edema.

Late in February, 1938, there appeared, quite suddenly, more than the usual amount of swelling. The patient remained in bed with the limb elevated. During the ensuing week he developed chills and fever. Three weeks later, April 11, 1938, having failed to improve, he was readmitted to St. Luke's Hospital.

Except for the left leg, the physical findings were negative.

On the posterior surface of the left thigh was a constricting cicatrix, 10 cm wide. It began just above the popliteal space and extended proximally for a distance of 15 cm. The upper 4 to 5 cm of this scar were hyperesthetic, the remainder hypesthetic. Below the lower border of the patella, the portion of the limb innervated by the sciatic nerve was completely paralyzed and anesthetic. The soft tissues here were markedly swollen. They did not pit but had the brawny resistance usually associated with lymphedema. The ankle region was huge and fluctuant. Some of the fluid was removed for culture and microscopic examination.

MEASUREMENTS

	Left	Right
Midtarsal joint region	24 cm	20 cm
Maximum ankle circumference	48.8 cm	25.4 cm
Circumference of calf	43.8 cm	37.5 cm

The foot lay at rest in an inverted position. Manipulation of the foot revealed complete absence of supportive structures of the ankle joint, with resultant markedly increased range of motion. In addition, a distinct crunching type of crepitation was felt.

Roentgenologic Examination.—Confirmatory, roentgenologic evidence of the relaxation of the ankle joint, noted on physical examination, is found in the altered configurations of the joint. There is moderate separation of tibial and astragalar shadows in the mesial and anterior portions of the ankle joint. The foot is so plantar flexed that at the angle the AP view is taken, both the anterior and posterior lips of the articular surface of the tibia are visualized.

The size of the shadow cast by the soft tissues is increased, particularly in the lateral view. The increased density of the shadow about the ankle joint proper and obliteration of the shadow of the intermuscular fat planes, attests the presence of a joint effusion with rupture into the surrounding tissues. Disseminated throughout this effusion shadow are many discrete regions of greater density. (A) Their irregularity in size and shape is due to their origin. They were found to be particles of bone fractured from the joint surfaces and floating freely in the joint. In the lateral view, shadows of numerous discrete particles are clustered together along the plantar surface of the foot to form a well-circumscribed band (B). This is the sheath of the flexor hallucis longus tendon, distended with fragments of bone and blood.

Radiating spicules of periosteal new bone are seen along the mesial cortex of the tibia and lateral cortex of the fibula (C). There is some hazy increase in density of the interior of the lower 25 cm of the tibia. In the AP view of the lateral half of the tibial articulating surface, the bony articular cortex casts a dense, regular shadow. Mesially the shadow of the bony articular cortex is reduced in density. Here, there is a well-circumscribed region of moderately decreased density about 1.5 cm in diameter which is not seen in the lateral views (D). The shadow cast by the tip of the internal malleolus is irregularly eroded and the size of the malleolus reduced.

Evidence of marginal erosion of the cortex is seen in the lateral view of the anterior surface of the tibia (E) and in the AP view of the lateral surface of the tibia (F) and in the mesial surface of the astragalus (G). In the AP view, the shadow of the bony

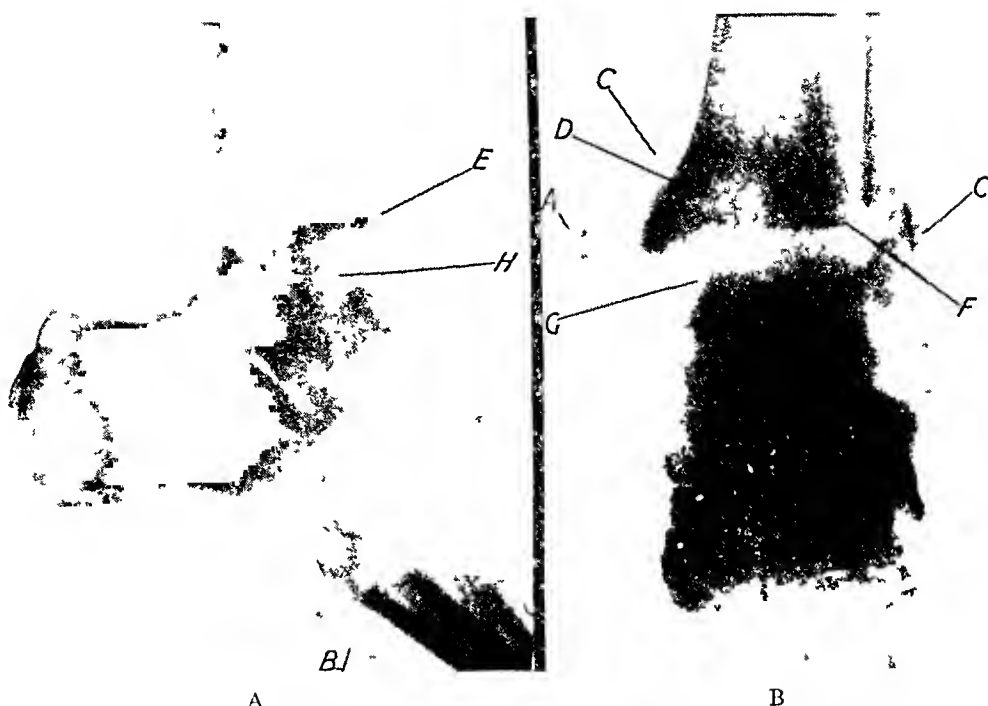


FIG 1—AP and lateral view of ankle. Disseminated throughout the soft tissue shadows are numerous discrete regions of greater density (A) the remnants of bony particles fractured from the joint surfaces. Similar particles filled the distended sheath of the flexor hallucis longus and their shadows form a discrete band (B) seen in the lateral view. Radiating spicules of periosteal new bone (C) are seen on mesial surface of tibia and lateral surface of fibula. A well circumscribed region of decreased density (D) is seen on the mesial articular surface of the tibia, laterally, the bony articular cortex casts a dense regular shadow. Marginal erosion is seen at E, F, G. The shadow of the bony articular cortex of the astragalus as seen in the lateral view is partially destroyed anteriorly. In the underlying bone there is an irregularly shaped region of decreased density about 1 cm in diameter (H).

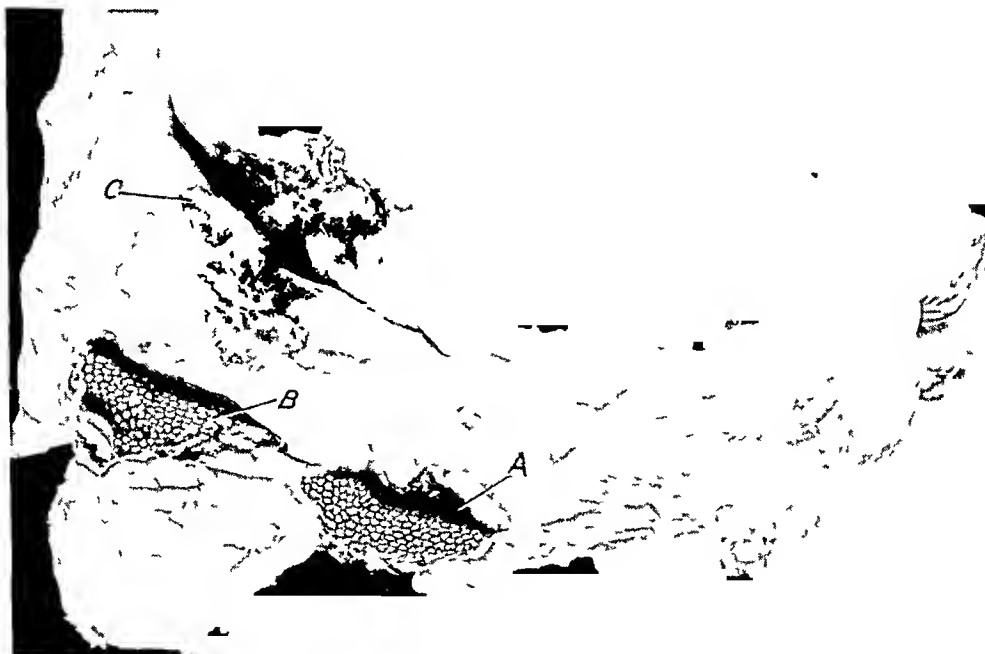


FIG 2—Photograph of the gross specimen with most of the soft tissues dissected away. The tendon sheath of the flexor hallucis longus (A) has been blocked out, and the nodules (B) studding its lining have been retouched. (C) An oval defect in the anterior mesial surface of the tibial cortex. Externally it communicated with the extensor tendons of the toes. Internally it communicated with a cavity in the tibia which is seen as region of decreased density (D) in Figure 1.

articular cortex is hazy over most of the articulating surface of the astragalus. The shadow of the bony articular cortex of the astragalus, as seen in the lateral view is partially destroyed, anteriorly. In the underlying bone there is an irregularly-shaped region of decreased density about 1 cm in diameter (H). The smaller tarsal bones and joints are essentially unchanged. *Roentgenologic Diagnosis* Neuropathic joint.

Laboratory Data R B C 3,490,000, Hb 12.4 Gm, W B C 10,000. Blood culture, neg., Wassermann and Kahn tests, neg., fluid aspirated from ankles, cultures, smears and stains for T B C and pyogenic organisms, neg. Sedimentation rate 15 mins 7 Mm, 30 mins 24 Mm, 45 mins 26 Mm, 60 mins 27 Mm.

Because of the complex clinical picture, that is, elephantiasis as a result of the constricting thigh cicatrix, loss of sensory and motor nerve supply throughout the sciatic distribution below the patella, and marked bone and joint changes, the leg was amputated at the knee May 4, 1938.

Pathologic Examination—Gross The specimen consisted of a lower limb, disarticulated through the knee joint, devoid of skin and subcutaneous tissues in the proximal 15 cm (stump flaps). The skin had the distinct "peau d'orange" appearance, and the soft parts the brawny resistance characteristic of lymphedema. There was no pitting edema. The diameter of the leg was increased throughout, being greatest in the ankle region where it measured 42 cm in circumference. The foot was in a moderately inverted position, dorsal and plantar flexion were increased, and there was a marked crunching crepitation associated with the abnormal, lateral motion which was present.

Beginning 3 cm above the internal maleolus, the sheath of the flexor hallucis longus was enlarged (Fig 2). It extended below the maleolus and forward along the plantar surface of the foot, to end 2.5 cm from the point of insertion of the tendon. It was filled with fragments of detached bone and clotted blood (Fig 1B). Connecting this sheath with the distended joint capsule, mesially, there was a sinus 0.5 cm in diameter. Another sinus extended out into the subcutaneous tissue, posteriorly, to end blindly. The wall of the sheath was 1.2 cm thick, and the lining was studded with myriads of nodules from 0.1 to 0.3 cm in diameter and elevated 0.1 to 0.2 cm.

Microscopically, the tendon sheath was composed of two quite distinct layers. The outer, 0.6 cm thick, was loosely arranged, edematous fibrous tissue. Disseminated throughout were numerous blood vessels. Lining each of these vessels was a single layer of cuboidal endothelial cells. Clustered about these capillaries were foci of chronic inflammatory cells, small round cells and plasma cells predominating. Some macrophages, containing large brown-staining granules were also seen.

The inner layer was also approximately 0.6 cm thick. The surface was thrown into folds comprising the nodules, seen grossly (Fig 2B). They consisted of myriads of closely packed erythrocytes, polymorphonuclear neutrophils, round cells and plasma cells lying in a loosely arranged fibrillar stroma. In addition, disseminated throughout, were spicules of dead bone then surfaces irregularly serrated. Near these spicules and in some instances lying in contact with them, were multinuclear giant cells of the foreign body type.

In the fatty and fibrous tissue below and behind this distended tendon sheath was an encapsulated hematoma about 3 cm in diameter. The sheath of the peroneus longus tendon was enlarged to as much as 1 cm in diameter throughout the 4 cm just opposite the distal end of the fibula. It was filled with fragments of detached bone and clotted blood and connected with the joint by a sinus 0.3 cm in diameter.

The capsules of the tibio-astragalal, subastragalal and fibula-astragalal joints were destroyed. Instead, one joint had been formed enclosed in a capsule which extended from the tibia to the calcaneus mesially, and from the fibula to the calcaneus laterally. It was filled with a viscid serosanguineous fluid, in which floated the astragalus and innumerable spicules of detached bone. The walls were 0.7 cm thick and covered with clotted blood.

The ankle joint was exposed by cutting in a coronal plane through both malleoli at about their midportions. In this manner the calcaneus, the astragalus, the distal 13 cm of the tibia and fibula as well as their respective joint surfaces were visualized (Fig 3A). For purposes of description, the bones and their joints were divided into the nine regions as indicated in Figure 3B (a microscopic slide of the entire region).

In this plane the foot was in a moderate, varus position. The mesial side of the tibia was, therefore, the weight-bearing portion. Here the hyaline articular cartilage was completely destroyed for 3 cm, the underlying bone had been gouged out to form a

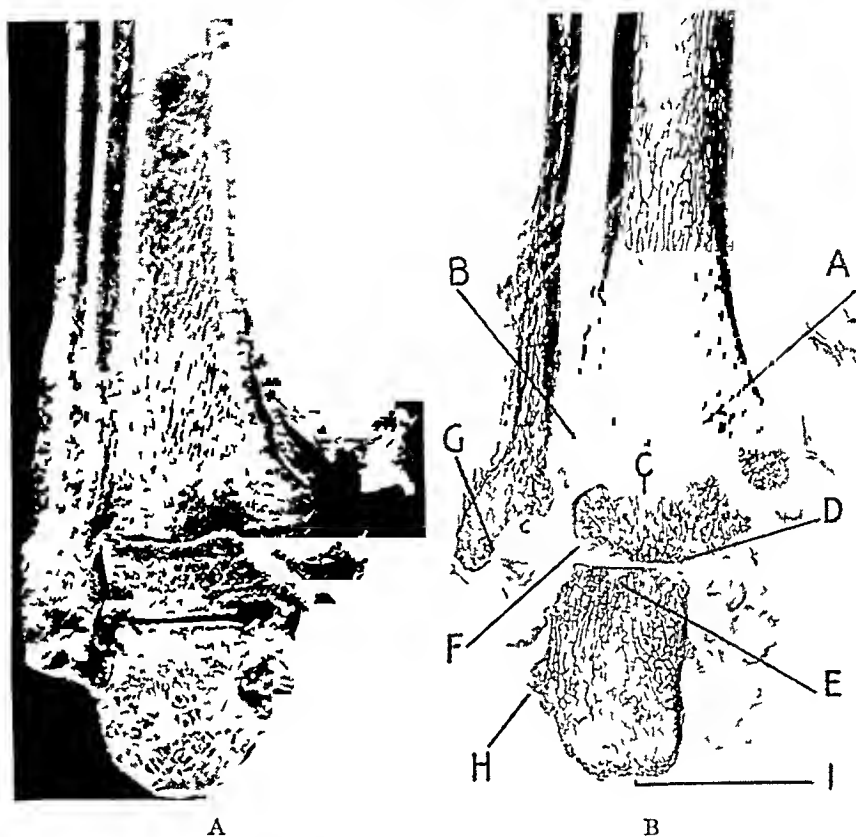


FIG 3—(A) A coronal section through the lower third of the leg and underlying tarsal bones. The plane passes through the posterior margin of the cavity seen at D in Figure 1. (B) A microscopic section through the same coronal plane. Photomicrographs were made of the designated regions.

pyramidal-shaped defect, its base 3 cm and its vertical height 2.5 cm (Fig 1D). The apex of this cavity opened through an oval defect in the cortex of the anterior mesial surface of the tibia and communicated with the sheaths of the extensor tendons of the toes (Fig 2C). Filling this cavity and the distended tendon sheaths was a mass of blood and detached fragments of bone.

The microscopic changes in the joint surface at region A of Figure 3B are shown in Figure 4. There was a marked destruction of bone and cartilage without attempt at bony repair.

Laterally, in the nonweight-bearing portion, the hyaline articular cartilage, although preserved, was deeply pitted and thinned out to 1 mm or less (region B, Fig 3B). Figure 5 is a photomicrograph of region B showing the junction of the mesial tibial cortex with the hyaline articular cartilage. The bone and cartilage were undergoing resorption by subchondral granulations. There was, however, a minimal amount of new bone formation.

The superior articulating surface of the astragalus was completely devoid of hyaline articular cartilage. The denuded spongy bone was stained red-brown with formalin-fixed blood and so shaped that the irregularities of its surface interdigitated with those of the tibia (region C, Fig 3B and A). The marked destruction of bone and cartilage of the

superior articulating surface of the astragalus is seen in Figure 6. As the astragalus was floating in the pathologic joint space, it was without a blood supply. Despite this fact, only the bone sand was without lacunar cells. Considerable new bone formation was present in the deeper portions. Calcification of these osteoid deposits would help produce the characteristic sclerosis seen in the roentgenograms.

The subastragal joint showed relatively few changes. The articular cartilage was deeply pitted and reduced to 0.1 to 0.2 cm in thickness (region D, Fig. 3B).

FIG 4



FIG 5

FIG 4—(Region A of Fig. 3 B). The bony articular cortex has been largely destroyed and only fragments of the calcified articular cartilage (A) remain. The marrow is densely fibrous and contains focal regions of round cell infiltration (B) as well as numerous spicules of bone sand (C). The surface of many of these latter is serrated with lacunae in some of which giant cell osteoclasts are seen (D).

FIG 5—(Region B of Fig. 3 B). Marginally, there is subperiosteal and subchondral invasion by a chronic type of granulation tissue (A) with destruction of the articular cortex and beginning invasion of the articular cartilage. Osteoblasts are seen on the surface of some of the trabeculae (B). The marrow is a mixed fatty and fibrous type (C). Focal regions of degeneration of the marrow do not show in these photomicrographs. Immediately beneath the cortex there are a few spicules of newly formed endosteal bone.

Figure 7 shows the region of transition from living to necrotic cartilage, on the inferior articulating surface of the astragalus. Where the bony articular cortex was intact, the overlying cartilage cells and matrix stained well (A). The bony trabeculae beneath this region were hypertrophied (B). These trabeculae cast a denser than normal shadow in the roentgenograms. Thus, they too would contribute to the sclerosed appearance of some of the bone. Immediately adjoining this was the lateral limit of the area of this surface of the astragalus, which received the maximum trauma. Here the

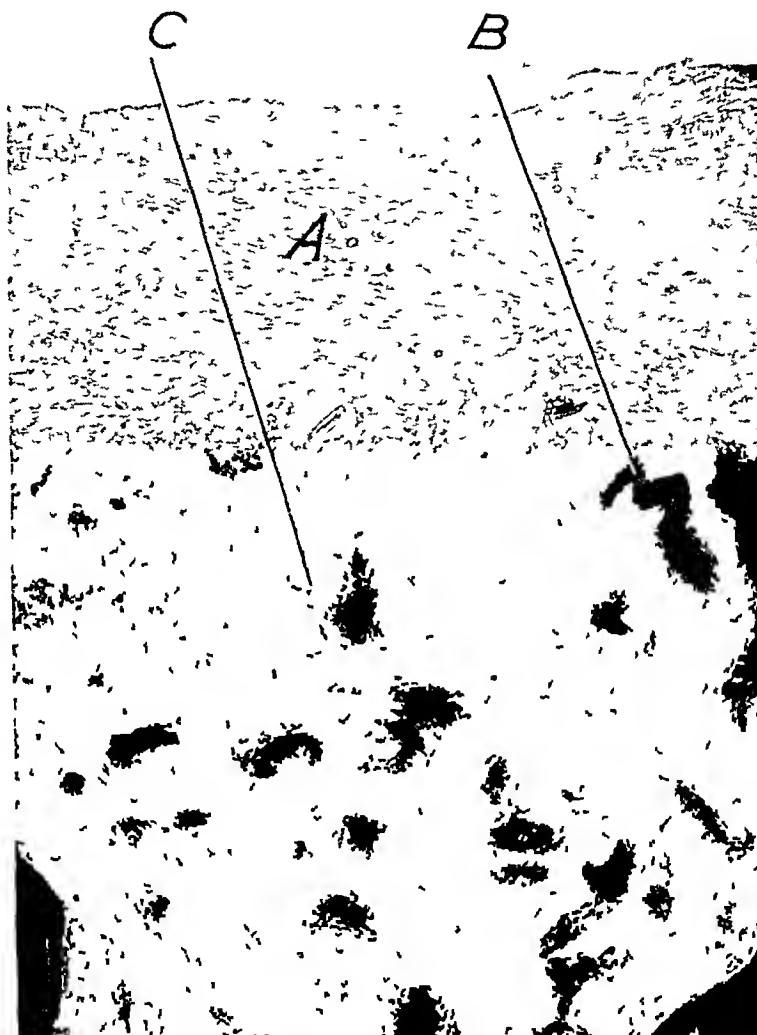


FIG 6—(Region C of Fig 3 B). The articular cartilage and bony articular cortex have been completely destroyed. Instead a densely fibrous type of tissue (A) covers the surface of the joint and fills the marrow spaces. In the depths are numerous fragments of so called bone sand (B) and considerable osteoid tissue (C). In most instances the particles of bone sand act as a nucleus for the osteoblasts' activity.

cartilage was necrotic, its cells and matrix staining very poorly. This necrosis was the result of interference of nutrition from the synovia, but mostly from trauma. Subchondral granulations were present throughout the entire extent of this necrotic cartilage. They had destroyed most of the bony articular cortex and invaded and thinned the cartilage by absorption from below. Their presence here, as in rheumatoid and tuberculous arthritis, is best explained as a foreign body reaction to sequestrate and attack the necrotic cartilage.

Figure 8—region E, is a microscopic study of the opposing surface of the calcaneus. Regional hypertrophy of bony trabeculae, subchondral cavitation and marked destruction of the articular cartilage closely parallel the changes seen in degenerative arthritis.

A panus covered most of the articulating surface of the fibula and the marginal portion of the opposing surface of the astragalus. In the region of the panus, the cartilage had a fibrous appearance. The subchondral spongy bone of the tibia and fibula was stained red-brown with hemorrhage for a depth of as much as 15 cm. A similar discoloration was present throughout most of the astragalus and calcaneus. There was

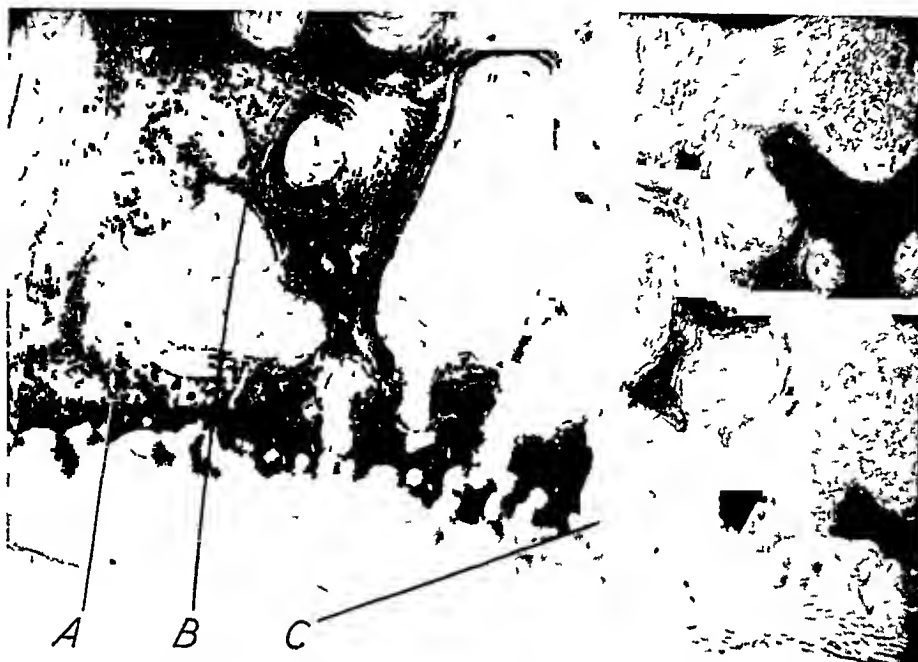


FIG 7—(Region D of Fig 3 B) The articular cartilage is markedly thinned and its surface irregular and fibrous. In some places the bony articular cortex remains intact (A) and the underlying bony trabeculae are hypertrophied (B). In neighboring places (C) there is a densely fibrous type of granulation tissue which has destroyed the articular cortex and is invading and resorbing the overlying cartilage. Focal regions of degeneration and round cell infiltration are present but not seen at this power. Where the articular cortex is intact the articular cartilage stains well, where it is absent the articular cartilage stains poorly.

a subperiosteal bony thickening, some of which was ossified. This extended along the distal 9 cm of the lateral surface of the fibula and distal 8 cm of the mesial side of the tibia (X of Fig 3A and B).

Figure 9 (region F of Fig 3B) shows the inferior marginal portion of the lateral articular surface of the astragalus. Destructive changes were minimal, as this region was subjected to relatively little trauma.

Figure 10 (region G of Fig 3B) shows the articular surface of the fibula. Despite the fact that this region was subjected to relatively little trauma, the changes in the cartilage were marked. A panus, containing numerous foci of round cells, covered the surface of the articular cartilage and was invading and destroying it. Subchondral invasion by granulations was minimal. These changes closely resemble those seen in proliferative arthritis.

Figure 3B—region H, shows a spur of periosteal new bone on both sides of the calcaneus. It was situated at the point of attachment of the joint capsule. These spurs were the result of elevation of the periosteum by the over distended and relaxed joint capsule. Figure 11 is a high power magnification, showing the lateral, periosteal spur and the underlying foci of endosteal new bone.

As a result of the peculiar gait of the patient, the base of the calcaneus was repeatedly traumatized. Evidence of this trauma is seen in the formation of periosteal new bone (region I, Fig 3B and Fig 12). This new bone may be likened to a very early calcaneal spur.

Lining the joint capsule is a markedly cellular and vascular granulation tissue. Disseminated throughout are numerous particles of bone sand, their lamellae devoid of cells and their edges deeply serrated by the osteoclastic activity of the surrounding granulation tissue. Present, also, are numerous large- and medium-sized foci of round cells giving it much the same appearance as has the synovial lining in rheumatoid arthritis.



FIG 8—(Region E of Fig 3 B) (A) is the subcortical cavity seen in Figure 3 B. It contains an inflammatory type of exudate (B). The overlying cartilage (C) and bony articular cortex (D) are largely destroyed. Laterally, the bony trabeculae are hypertrophied (E), medially, the margins of the trabeculae are serrated, the marrow is fibrous and there is bone resorption (F).

Discussion—There are three theories of pathogenesis advanced to cover some or all cases of neuropathic joints. The first, the chief proponents of which are Herndon,¹¹ McCallum¹² and Staigardt,¹³ contend that neuropathic joints in tabetics develop as a result of injury to a nerve and a low grade spirochetal infection of the joint itself. Opposing this theory are the following facts. Careful search, in a large number of cases, has failed to reveal either the spirocheta pallida or other evidence of syphilitic infection, there is both clinical and experimental evidence that certain other factors, common to tabes and to syringomyelia, are really responsible for the development of neuropathic joints, the joint lesions seen in conjunction with syringomyelia and peripheral nerve injuries are similar in all respects to those present in Charcot's joints.

The second, the trophic theory, considers some disturbance in the nervous trophic regulatory mechanism as the factor of prime etiologic importance. In support of this theory, Wartenberg¹⁴ cites the following pathologic alterations as being present in the neighborhood of unilateral Charcot's joints. Elevation of local temperature, rise in venous pressure, increase in oscillometric index, anomalies of sweat secretion, and disturbances in the pilomotor reflexes.

That the central nervous system exercises a profound influence on the nutrition of all tissues seems certain. There is, however, no evidence of special

nerves whose function is merely trophic. The complex influence exerted by the central nervous system is seen in the limbs of individuals with a residual postpoliomyelitis paralysis. The skin becomes tense, thin, shiny, cyanotic and cold. The striated muscles atrophy and the supporting structures about the involved joints relax. In children, the bones not only become less dense, as

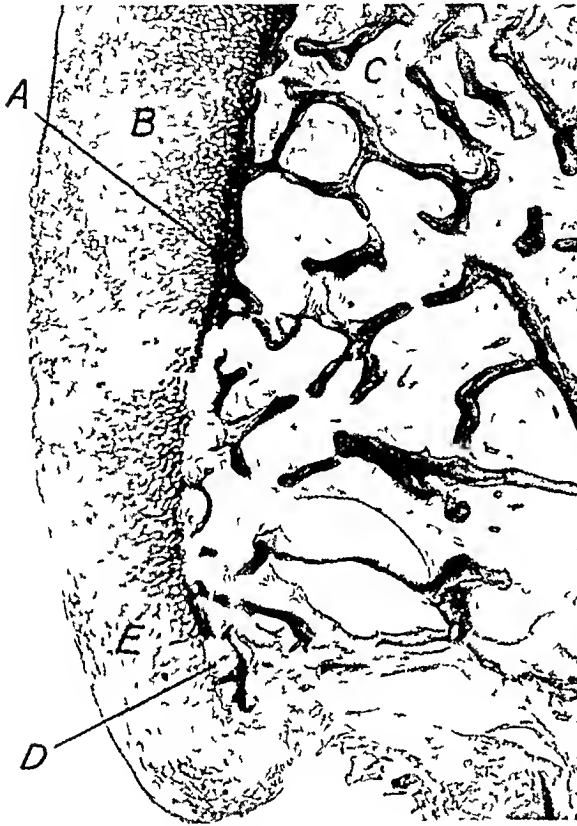


FIG 9—(Region F of Fig 3 B) Articular cortex (A) preserved overlying hyaline articular cartilage (B) stains well is of about the usual thickness and has smooth surface. Underlying marrow (C) is of fatty type. Marginally (D) there is subchondral invasion of articular cartilage and marked destruction of articular cortex. Here, the overlying articular cartilage (E) is thinned, stains poorly and its surface is slightly roughened.

demonstrated roentgenologically, but also decrease in circumference, a process known as concentric atrophy. Yet, despite these marked "trophic" changes, neuropathic joints do not develop. Sensation, the loss of which is common to all neuropathic joints, remains intact in poliomyelitis. As the individual is not ataxic, joint injuries are uncommon. In addition, once an injury occurs, the attendant pain causes the individual to protect the part and thus allow it to heal.

The third, the mechanical theory, contends that neuropathic joints are the result of trauma to a joint, deprived of its sensation.

The results of severe trauma are so well-recognized, they need no comment. That prolonged trauma of a milder nature frequently produces bony changes is not as well-recognized. Brailsford¹⁵ and Kuntscher¹⁶ have published roentgenograms showing the effect upon bones of pro-

longed rhythmic trauma produced by pneumatic tools. In Brailsford's patients, well-circumscribed regions of decreased density developed in the metacarpals and carpals. Kuntscher¹⁶ believed the bony disintegration he found in the weight-bearing portions of the condyles and head of the femur closely paralleled osteochondritis. As the nerve supply remained intact, these cannot be considered neurotrophic lesions.

Many individuals with classical tabes dorsalis, including ataxia, hypotonia and loss of deep joint sensibility, never develop neuropathic joints. Others, with bilateral sensory changes develop only unilateral neuropathies. In the latter, a history of trauma to the afflicted limb can usually be elicited. The severity of the injury is overlooked because of the absence of pain. Inadequate treatment results in the rapid development of a neuropathic joint. That

loss of joint sensation alone does not result in the development of neuropathic joints in the human is, therefore, apparent. That destruction of joint sensation by cutting the posterior roots does not suffice to produce a neuropathic joint in dogs, cats, or rabbits has been repeatedly confirmed^{17, 18, 19}

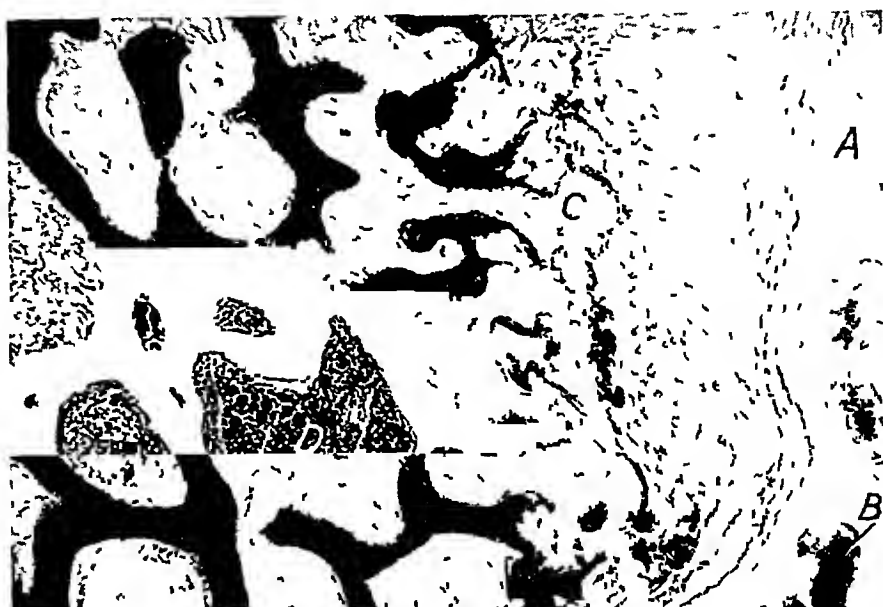


FIG 10—(Region G of Fig 3 B) The surface of the articular cartilage is covered by a panus (A) which is invading and destroying the cartilage. Disseminated throughout this panus are foci of round cells (B). Regionally, the bony articular cortex has been destroyed by an immature type of subchondral granulation tissue (C) which, in addition, is invading and destroying the articular cartilage from below. The marrow (D) is of a mixed fatty and fibrous type. A layer of osteoblasts covers the surface of many of the trabeculae.

The case under consideration supports the mechanical theory. Severance of the sciatic nerve resulted in the development of a combined motor and sensory lesion. Changes appeared in the form of marked atrophy of the leg muscles and relaxation of the ankle joint due to loss of motor nerve supply. The sensory loss was characterized by a marked ataxia and anesthesia below the knee. The trauma, associated with the act of walking upon such a limb, was often excessive because of the absence of the protective sense of pain. This was sufficient to cause the joint to disintegrate.

Roentgenograms of the ankle joint revealed changes typical of those ascribed to neuropathic joints. There was marked destruction of the opposing joint surfaces with some sclerosis but no atrophy. Disseminated throughout the markedly enlarged joint were numerous fragments of bone. An unusual feature was the extra articular migration of the bone sand causing the shadows in the roentgenograms. As a result of stripping of the periosteum, by the distended capsule, radiating spicules of new bone were present on the lateral surface of the fibula and mesial surface of the tibia.

SUMMARY

A case is reported of severance of the sciatic nerve at mid thigh, paralyzing the muscles of the leg and causing a loss of sensation to foot and back

of leg Following active use of the limb, a neuropathic arthropathy developed in the ankle joint The leg was amputated, and the diagnosis confirmed by pathologic examination The case substantiates the theory that the changes are the result of excessive trauma to a relaxed anesthetic joint and favors the same theory of pathogenesis of these joints in tabes and syringomyelia

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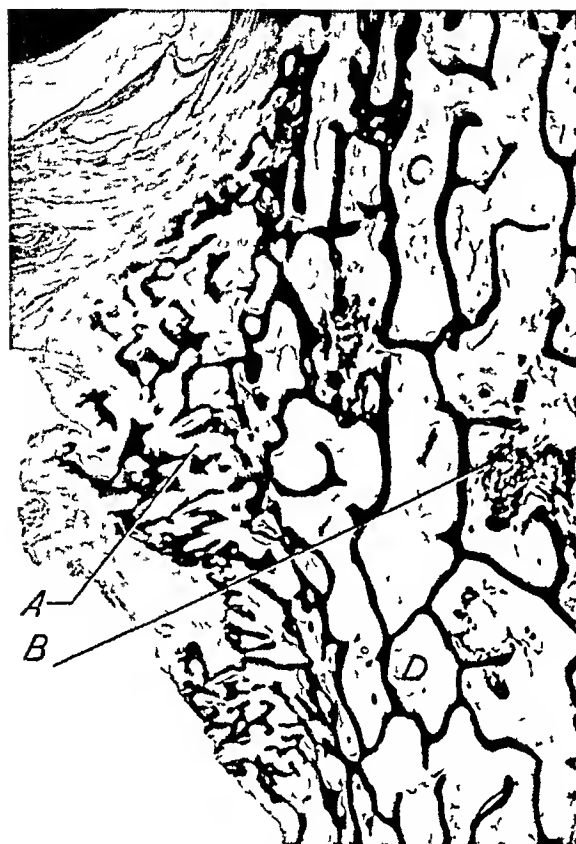


FIG 11—(Region II of Fig 3 B) The results of trauma attendant on the stretching and tearing of the capsule and ligaments are seen in the ossification of the external lateral ligament at its point of attachment to the calcaneus Here, there is a spur of periosteal new bone (A) as well as several foci of endosteal new bone (B) At the level above the endosteal reaction the marrow is fibrous (C) whereas below, the marrow is the usual fatty type

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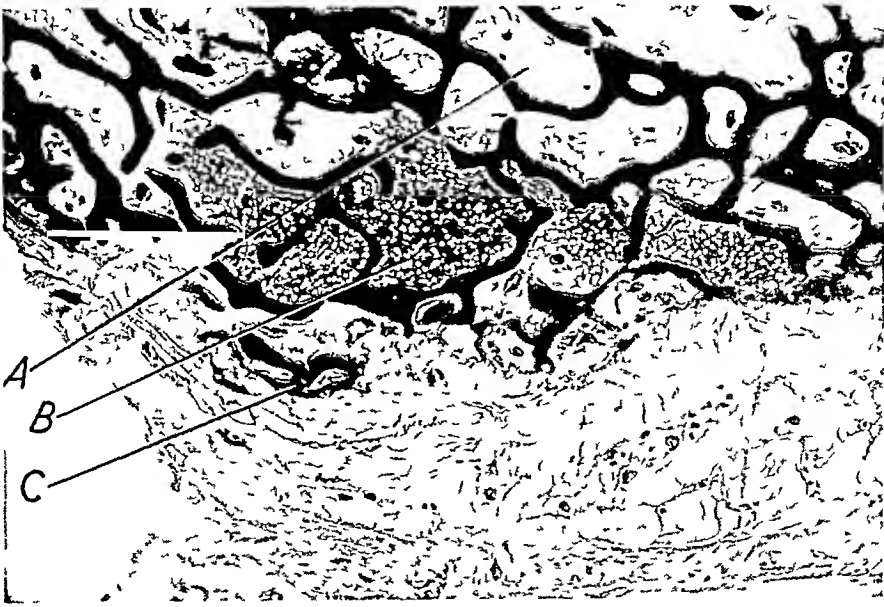


FIG 12 —(Region I of Fig 3 B) The cancellous spaces are filled with a fatty marrow (A) with the exception of the narrow strip of hematopoietic marrow (B). Some periosteal new bone formation is seen at C, the region which received the maximum traumatization. This latter may be likened to a beginning calcaneal spur.

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PRIMARY RETICULUM CELL SARCOMA OF BONE

REPORT OF TWO CASES WITH BONE REGENERATION FOLLOWING ROENTGENOTHERAPY

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UNTIL RECENTLY reticulum cell sarcoma of bone has been considered a secondary lesion. That this neoplasm may be primary in bone was first demonstrated by Oberling⁵ in 1928. Adequate corroboration of this thesis did not appear, however, until the recent publication of Parker and Jackson.⁶ These authors reported 17 cases of bone tumor, including 13 cases from the Registry of Bone Sarcoma of the American College of Surgeons, in which they made the diagnosis of primary reticulum cell sarcoma. Most of these cases had been classified previously as osteogenic sarcoma, Ewing's sarcoma, Hodgkin's disease, lymphosarcoma, or inflammation. After careful review, Parker and Jackson believed each of these lesions identical histologically with reticulum cell sarcoma as seen in soft tissue, but pointed out certain characteristic differences in the clinical course. Simmons,⁷ in a recent article, and Kuhns, *et al*,⁴ in the Sixty-ninth Report of Progress in Orthopedic Surgery, also discussed this group of tumors as primary lesions of bone. According to Ewing,³ some of the 17 cases of pure reticulum cell sarcoma of bone reported by Craver and Copeland² were primary in this tissue. The Committee of the Registry of Bone Sarcoma also has recognized reticulum cell sarcoma arising in bone marrow as a distinct entity, and has recommended inclusion of this term in the newly proposed classification³ of tumors of bone.

In the Peiping Union Medical College Hospital we have observed two cases which belong to this group of primary bone tumors, and consider them of sufficient interest to warrant reporting.

CASE REPORTS

Case 1—A Chinese girl, age 21, was first seen April 30, 1932, in the Tumor Clinic of the P U M C Hospital, and complained of a swelling of the left shoulder region, which had been present for more than two months. From the beginning of 1930 she had experienced occasional pain shooting from the fingers to the shoulder on the left side. The pain occurred from one to four times a month, and lasted from a few minutes to a few hours on each occasion. In February, 1932, the patient noticed a steadily increasing swelling in the left shoulder region accompanied by constant pain, and a mass in the left arm pit. The motion of the left shoulder became gradually impaired until the loss of function was complete. Numbness in the left upper extremity was never present.

There was no history of sore throat, bleeding from the nose, headache, chronic

SARCOMA OF BONE

PLATE I



Fig 1



Fig 2



Fig 3



Fig 4

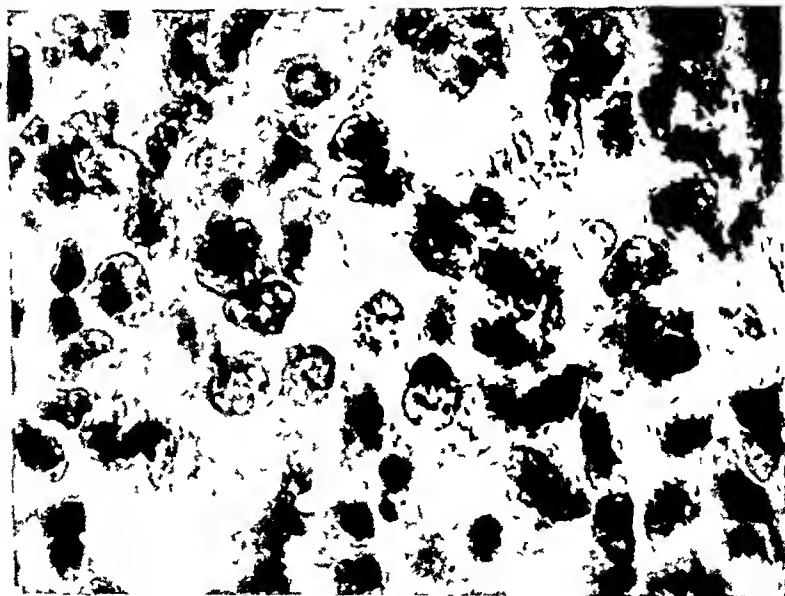


Fig 5

FIGS 1 and 2—Case 1 Appearance of the tumor before treatment. Note the diffuse swelling of the shoulder and the neck and the mass in the axilla. The arm was slightly abducted.

FIGS 3 and 4—Case 1 Appearance of the tumor bearing regions, six years and three and a half months after treatment. Note the small nodule of fibrous tissue in the axilla that has been stationary in size for several years. The atrophy of the shoulder muscles is evident.

FIG 5—Case 1 Photomicrograph of a cervical lymph node showing reticulum cell sarcoma before treatment. The tumor cells and their nuclei vary in shape, size and staining. The characteristics of a normal lymph node are absent. Hematoxylin eosin stain ($\times 1,400$).

cough, hemoptysis, or tumor elsewhere in the body. The general health apparently was not affected by the present illness. There was no history of cancer in the family.

Physical Examination—The patient was well-developed and well-nourished, she

PLATE II



Fig 6



Fig 7



Fig 8



Fig 9

FIG 6—Case 1. Roentgenogram of the left shoulder taken June 30, 1932 just before radiation treatment. Note the marked destruction of the entire scapula, also the lateral end of the clavicle and early erosion of the proximal portion of the lateral cortex of the humerus.

FIGS 7 and 8—Case 1. Roentgenograms showing the changes in the involved bones during and following the radiation treatment. Figure 7, taken July 16, 1932, 12 days after the beginning of the therapy, note that the mild erosion of the lateral cortex of the upper end of the humerus has definitely increased. Figure 8, taken August 29, 1932, shows progressive bone regeneration after the first course of radiation.

FIG 9—Case 1. Roentgenogram taken November 19, 1938, showing the stationary condition of the regenerated bones.

appeared to be slightly pale, but was not suffering from acute discomfort. A large, diffuse swelling of the left shoulder was present involving the clavicular, supraclavicular, deltoid and scapular regions (Figs 1 and 2). The tumor was hard in consistency, fixed, ill-defined and not tender. The overlying skin was diffusely red but not adherent.

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The left axilla contained two firm, nodular, movable masses measuring 5 and 1.5 cm in diameter, respectively. In the left lower cervical and supraclavicular regions, along the medial border of the tumor, were many firm lymph nodes, each about 2 cm in diameter. The left shoulder joint could not be moved. Sensory changes in the left upper extremity could not be detected. Motion at the elbow and wrist was normal. Roentgenograms showed extensive destruction of the entire left scapula, marked destruction of the lateral end of the clavicle, and partial destruction of the upper end of the humerus (Fig 6). Evidence of pulmonary, pleural or mediastinal metastasis was not present. Examination of other regions of the body was essentially negative. One of the enlarged lymph nodes in the left lower cervical region was removed and the histologic diagnosis was reported as lymphosarcoma (Fig 5). The lesions in the bones were considered to be secondary in nature. Recently, at the suggestion of Dr H T Kimm, this case was reviewed, and in the light of current knowledge concerning the subject herein dealt with, the diagnosis was changed to primary reticulum cell sarcoma of bone with metastasis in the regional lymph nodes.

On July 4, 1932, the tumor was observed to be considerably larger and several new masses, each about 2 cm in diameter, were found in the subcutaneous tissue of the cervical and scapular regions on the right side. Examination of the blood showed 80 per cent hemoglobin (Sahli), and normal red, white, and differential counts. Abnormal leukocytes were not found. Weight 41.7 Kg. The blood Wassermann reaction was negative. A test for the presence of Bence-Jones protein in the urine was not carried out.

A series of roentgen ray treatments were administered between July 7, and September 7, 1932 (Table I). The pain gradually disappeared and the swelling began to regress 12 days after the therapy was started. A roentgenogram taken at this time showed increased erosion at the surgical neck of the humerus (Fig 7). On July 30, 1932, definite improvement of the involved bones with evidence of regeneration of bone was first observed roentgenologically. On August 5, 1932, the patient complained of dull pain in the left elbow. Examination showed enlargement of the left epitrochlear nodes and roentgenologic evidence of a small area of rarefaction in the lateral cortex near the distal end of the humerus, these lesions subsequently disappeared following roentgenotherapy (Table I, Part VI). On August 16, new tumor nodules appeared in the posterior inferior axillary and infrascapular regions on the left side. These nodules regressed completely after roentgenotherapy (Table I, Part VII).

The blood picture on repeated examinations remained satisfactory. Chemical analysis of the blood showed, on August 2, 10.9 mg per cent of calcium, 6.1 mg per cent of phosphorus, and 0.42 and 0.72 units of phosphatase in two different specimens, on August 23, 11.4 mg per cent of calcium, 4.3 mg per cent of phosphorus, and on August 29, 11.4 mg per cent of calcium and 4.0 mg per cent of phosphorus.

The therapy produced progressive regression of all the lesions and by September 20, 1932, complete regression of the tumefaction had occurred with the exception of the anterior axillary mass which was then 3 cm in diameter and of a small firm node in the left supraclavicular region. Repeated roentgenologic examinations showed progressive reossification of the involved bones (Fig 8).

Between December 30, 1932, and January 23, 1933, a second series of roentgen ray treatments were administered through two fields in the left shoulder and one field in the left cervical region (Table II). The general condition remained satisfactory, and on February 14, 1933, the patient's weight had increased to 45.8 Kg. On May 16, 1933, the residual mass in the left anterior axillary region was noted to have become larger. Fifteen seeds of 0.3 Mm Au in wall thickness, each containing 1.16 mc of radon, were inserted around this nodule, five seeds of 1.25 mc each were inserted into the left supraclavicular space (June 20, 1933). A biopsy secured at this time from the axillary mass, by means of a Hoffman's punch, did not show the presence of tumor.

Subsequently, the patient has been examined from time to time. There has been no evidence of recurrence or metastasis of the tumor. The small nodule in the left

axilla has been stationary, apparently consisting of a mass of fibrous tissues (Figs 3 and 4) The muscles of the shoulder have become atrophic and the motion of the joint limited The left arm can be raised anteriorly to 90° , posteriorly to 45° , and in abduction to about 60° The roentgenologic study on the occasion of the last visit, February, 1940, revealed the regenerated bones to be in good condition (Fig 9) The patient is in apparently perfect health seven years and seven months after the institution of treatment

PLATE III



Fig 10



Fig 11



Fig 12



Fig 13

FIG 10—Case 2 Appearance of the tumor before treatment

FIG 11—Case 2 Roentgenogram of the mandible before treatment Note the marked destruction of the ramus The condyloid process cannot be visualized

FIG 12—Case 2 Normal appearance of mandibular region one month following radiation treatment

FIG 13—Case 2 Roentgenograms of the mandible seven months following radiation treatment Note the regeneration of the destroyed ramus

Case 2—A Chinese housewife, age 59, was first seen in the Surgical Clinic of the P U M C Hospital, June 18, 1938, complaining of a swelling in the left preauricular region for three months, and local pain in the same area for two months The pain was dragging or burning in character and occurred only occasionally During the previous month, the patient had experienced numbness in the left half of the lower lip Trismus or dysphagia was not present There was no history of nasal obstruction or bleeding The general health was not affected by the present illness Five years previously the patient had suffered from "toothache" for which most of her teeth had been extracted There had been an area of swelling in the thyroid region since the age of 16

Physical Examination—The patient was well developed, well nourished and did not appear ill The face was asymmetric due to the presence of a round, firm swelling,

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TABLE I
ROENTGENOTHERAPY
Case 1 First Series

Date 1932		Dosage in r to Port*						
		I	II	III	IV	V	VI	VII
July	7	56						
	8		40					
	9	40						
	11		40					
	12	40						
	13		40					
	14	40	40					
	15	40	40	132	132			
	16	40	40					
	18	40	40	132	132			
	19	40	40					
	20	40	40	132	132			
	21	40	40					
	22	80	80	132	132			
	23	80	80					
	25	80	80	132	132			
	26	80	80					
	27	80	80	132	132			
	28	80	80			160		
	29	80	80	132	132			
	30	80	80			160		
Aug	1	120	120	172	172			
	2	60	60			160		
	3	60	60	132	132			
	4	40	40					
	5		40	88	88			
	6		40			160	200	
	8		80	110	110			
	9		40			160	200	
	10		40	88	88			
	11		40			160	200	
	12			88	88			
	13					80	200	
	16					120	200	
	18						120	160
	20						80	160
Sept	23						120	160
	25						80	160
	27						80	160
	30							160
	1							160
	3							80
	6							120
	7							80
Total		1,336	1,600	1,602	1,602	1,040	1,480	1,400
							Grand total	10,060

Factors of therapy
Voltage 160 K V
Current 10 M A
Filter 56 Mm oil
0 25 Mm Cu
1 5 Mm Al
Skin target distance 50 cm
Intensity 23 7 r per minute measured in air

- * Port I Left shoulder and supraclavicular region anterior
Size 15x20 cm
Port II Left shoulder and scapular region posterior
Size 20x20 cm
Port III Right supraclavicular cervical and supraspinous regions anterior
Size 8x10 cm
Port IV Same as Port III, posterior
Size 10x12 cm
Port V Left cervical lateral
Size 8x8 cm
Port VII Left middle back posterior
Size 11x14 cm

7 cm in diameter, which was fixed to the ramus of the mandible on the left side (Fig 10). It was slightly tender. The overlying skin appeared normal. There was an enlarged, firm but freely movable lymph node, 2 cm in diameter, just behind the left angle of the mandible. Enlarged lymph nodes were not found elsewhere. Hypoesthesia was present in the left half of the lower lip. Inside the mouth, the area of swelling could neither be seen nor palpated. The uvula was deviated slightly to the right. The tonsils and the nasopharynx were normal to inspection and palpation. Many teeth were missing, the remaining few were dirty and carious. A benign goiter was present. The liver and spleen were not palpable. Mild hypertension existed. Examination of the blood showed 94 Gm per cent of hemoglobin and normal cell counts. Abnormal leukocytes were not found. Other laboratory data were not obtained.

Roentgenograms revealed a marked destructive lesion in the left ramus of the mandible (Fig 11). Tissue aspirated from the mass was thought questionably to be lympho-epithelioma. When the case was restudied recently, the diagnosis of reticulum cell sarcoma seemed evident (Figs 14 and 15).

TABLE II
ROENTGENOTHERAPY
Case 1 Second Series

		Dosage in r to Port*			KV †
Date		I	II	III	
Dec	30 1932	208	208	208	160
Jan	3 1933	208	208	208	"
	5	208	208	208	180
	7	208	208	208	"
	9	208	208	208	"
	13	156	156	156	"
	16	104	104	104	"
	18	78	78	78	"
	20	52	52	52	"
	23	104	104	104	"
Total		1,534	1,534	1,534	

* Port I Left shoulder axilla and supraclavicular region anterior
Size 12×16 cm
Port II Left shoulder and scapula
Size 20×20 cm
Port III Left cervical region
Size 9×10 cm

† The factors were the same as in the first series (Table I)

Daily roentgen ray treatments were started on July 11, 1938, using a large field which included the mandible as well as the entire cervical region on the left side. Later, the field was reduced and the radiation confined to the tumor and its immediately adjacent tissues (Table III). A total dose of 4,481 r was delivered in 49 days. The pain disappeared and the tumor began to regress rapidly one week after the treatment was started. By the end of the treatment, on August 29, 1938, the tumor had disappeared completely (Fig 12). The enlarged lymph node in the left upper cervical region disappeared three weeks later. The skin tolerated the therapy well. In September, 1938, roentgenologic examination revealed that the lesion in the mandible had improved markedly. This change was progressive as demonstrated at another roentgenologic examination on April 17, 1939 (Fig 13). The last examination, on April 24, 1940, showed no evidence of local recurrence or metastasis. The function of the lower jaw was normal. The patient is in good health and has no complaint.

Discussion—According to Parker and Jackson, 77 per cent of all cases of primary reticulum cell sarcoma of bone occur in patients under the age of

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40, and 35 per cent under the age of 20 years, although any age-group may be affected. The disease usually occurs in the long or flat bones. The onset is similar to that of osteogenic sarcoma but the subsequent course differs greatly. The most common initial symptom is pain unrelieved by rest and

PLATE IV

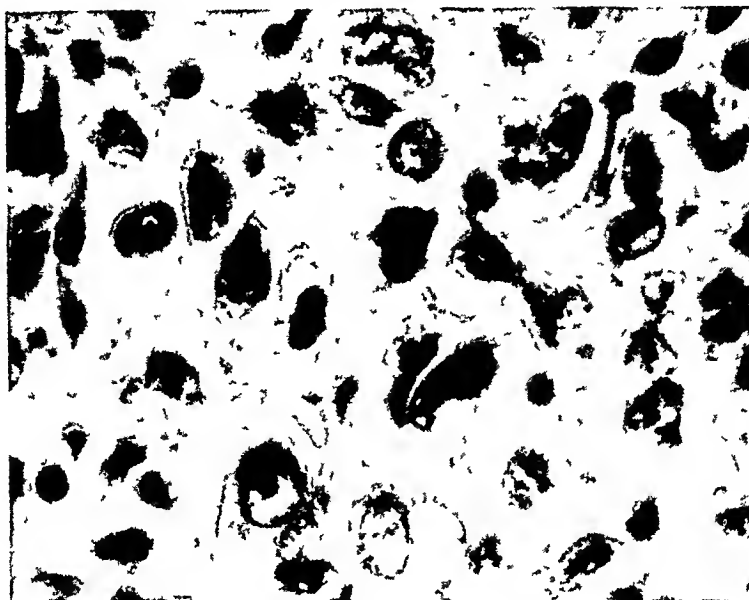


Fig 14

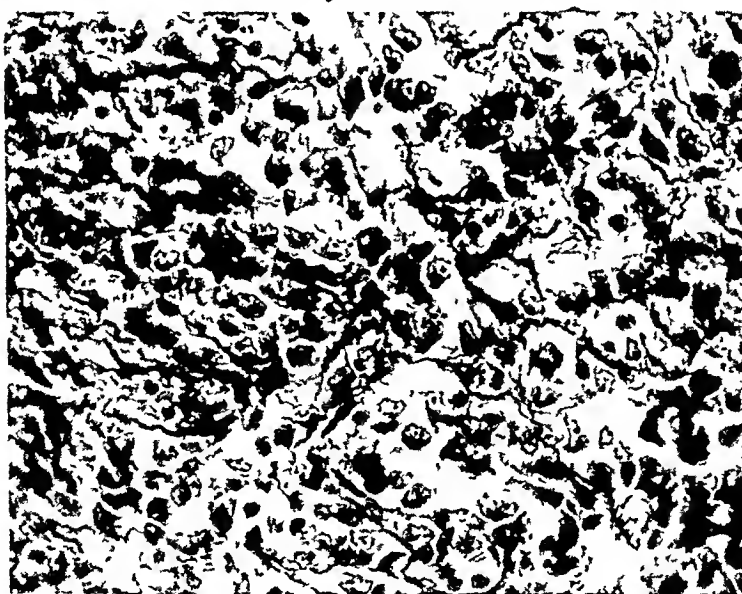


Fig 15

FIG 14—Case 2 Photomicrograph of the tissue aspirated from the mandibular tumor before treatment, showing reticulum cell sarcoma. Hematoxylin-eosin stain ($\times 1,370$)
FIG 15—Case 2 Photomicrograph of the same tissue shown in Figure 14. Toot's silver stain for reticulum ($\times 567$)

localized at the site of the primary lesion or referred to the adjacent joint. Sometimes a painless swelling may be the first complaint. Not infrequently a pathologic fracture occurs before treatment is sought. In the majority of cases, tumefaction of the affected part is present at the time the patient is

first seen. The tumor may grow very rapidly and attain considerable size, involving the surrounding soft tissues. Metastasis occurs comparatively late and usually affects the regional lymph nodes rather than the lungs. Metastasis to bones occurs but infrequently. These characteristics are in contradistinction to the generalized spread which usually occurs relatively early in the course of reticulum cell sarcoma of the soft tissues.

While the lesion appears locally extensive and highly malignant, it seldom affects the general condition of the patient as does osteogenic sarcoma, and

TABLE III
ROENTGENOTHERAPY

Case 2

Date 1938	Dosage in r to Port* I	Date 1938	Dosage in r to Port† II
July 11	102	Aug 3	145
12	102	4	145
13	102	5	145
14	122	9	145
15	122	10	145
16	122	11	145
18	122	12	145
19	122	15	145
20	122	16	170
21	122	20	145
22	122	22	145
25	122	23	145
26	122	24	145
27	122	25	145
28	122	26	145
29	122	29	145
Aug 1	122		
2	122		
3	122		
Total	2,136	Total	2,345
		Grand total	4,481

Factors of therapy

Voltage	180 K V
Current	8 M A
Filter	56 Mm oil 0.5 Mm Cu 2.0 Mm Al
Skin target distance	50 cm
Intensity	17 r per minute

* Port I Left half of mandible and entire left cervical region lateral
Size 20x16 cm

† Port II Posterior half of body and entire ramus of mandible and the upper
cervical region lateral
Size 10x10 cm

it is amenable to appropriate treatment. The roentgenographic appearance of the lesion is not characteristic. In the early stages, only mottled areas of destruction in the medulla may be observed. In more advanced cases marked osteolysis and rarely osteogenesis can be seen. Histologically, the structure is identical with that of reticulum cell sarcoma of a lymph node or other soft part.

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Among primary bone lesions, reticulum cell sarcoma should be differentiated from Hodgkin's disease, lymphosarcoma, Ewing's sarcoma, osteogenic sarcoma, and osteomyelitis. As pointed out by Parker and Jackson, the histologic picture usually is sufficient for differentiation, in doubtful cases the clinical course will lead to the correct interpretation. Primary Hodgkin's disease and true lymphocytoma of bone are extremely uncommon. Osteogenic sarcoma and osteomyelitis do not respond favorably to radiation therapy.

We believe that the cases described herein fulfill the criteria outlined by Parker and Jackson. In the first one, since only a cervical lymph node was secured for histologic examination, the diagnosis of primary reticulum cell sarcoma of the scapula may be questioned. However, the favorable clinical course following treatment, the localization of the growth and the lack of evidence suggesting the presence of a primary lesion elsewhere, all indicate that this was a primary lesion of bone. It would be most improbable that an unrecognized primary lesion, if there had been such, would have remained concealed for more than seven years after the lesion in the scapula had been controlled by radiation.

Parker and Jackson found that early amputation followed by radiation of the adjacent lymph nodes yielded the best results. Three of their cases were treated by radiation alone. One of these patients died of the disease within two years and the other two were living for one and three years respectively, with the disease unchecked. In three other cases initial radiation was administered but, due to either local recurrence or metastasis to lymph nodes, subsequent amputation was performed. These patients were living and apparently well ten to 14 years later. The details of the radiation were not given. These data appear to show that radiation alone does not constitute effective treatment.

The results of irradiation in our cases, on the other hand, were distinctly encouraging. In both instances, the primary as well as the secondary lesions exhibited marked radiosensitivity, and complete regeneration of bone ensued after the disappearance of the tumor. The first patient is living and well, apparently free from the disease, seven years and seven months, and the second patient one year and eight months, after the treatment was completed. In our first case, there could have been no other choice of therapeutic measure, as the lesion was so extensive and so located that even the most radical surgical procedure could not have eradicated the disease. In the second case, hemisection of the mandible and wide removal of the neighboring soft tissues as well as of the cervical lymphatics could have been considered. However, we believe that in the management of such radiosensitive lesions, irradiation rather than surgery is the method of choice. For lesions of the long bones, amputation may yield equally good results. On the other hand, even in such instances radiation may be tried first without harm. In the three cases reported by Parker and Jackson in which radiation failed to arrest the disease, subsequent surgical attack effected an eventual cure.

The success of irradiation may depend primarily on the method of application. In general, protracted, fractionated irradiation is preferred with the total dosage brought up to the maximum, according to the size, location and distribution of the given lesion. In our cases, a total dose of 4,000 to 5,000 r was delivered to the primary lesion, and 1,500 to 3,500 r to each of the metastatic lesions.

It is interesting to note the remarkable regeneration of the involved bones following irradiation. In the first case, the entire scapula had been destroyed and fragmented by the infiltrating tumor, its normal contour being lost completely (Fig 6). During the first two weeks of irradiation, there seemed to be even more decalcification or osteolysis (Fig 7). Reossification began in about three weeks and thereafter progressed steadily (Fig 8), even after the completion of the therapy. Complete regeneration occurred within a period of six to seven months, the scapula as well as the clavicle and the humerus resuming normal structural contour (Fig 9). Likewise, in the second case, the destroyed portion of the mandible regenerated following radiation (Figs 11 and 13). The mechanism of regeneration or reossification following irradiation of bone tumors is an interesting phenomenon. Baunschwig's¹ work on the repair of bone following irradiation in benign giant cell tumor is illuminating. But in cellular tumors, such as reticulum cell sarcoma in which the bone as well as the surrounding soft tissues are extensively destroyed, metaplasia within the tumor due to irradiation does not seem likely to play the principal rôle. The endosteal and periosteal elements also must suffer severe damage, and how their activity can be restored to reform a perfect bone is difficult to explain. It may be assumed, however, that the periosteum is not totally destroyed and that regeneration originates from this structure.

SUMMARY

Two cases of primary reticulum cell sarcoma of bone are presented.

The outstanding clinical features of the disease are (1) An extensive local lesion which appears out of harmony with the usual good general condition of the patient, (2) a comparatively benign course in spite of the highly malignant appearance of the tumor, and (3) a high degree of radiosensitivity which renders the lesion amenable to appropriate treatment.

Radiation was the only form of therapy employed in the two cases herewith reported. The first patient is living and well seven years and seven months, and the second patient one year and eight months, following the institution of treatment.

In the first case, roentgenotherapy effected complete regeneration of an extensively destroyed scapula, and resulted in the preservation of a useful limb. In the second case, the involved mandible reossified with good functional result.

The authors wish to thank Dr H. T. Kimm for his helpful suggestions in the preparation of this report.

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UROLOGY AWARD

The American Urological Association offers an annual award 'not to exceed \$500 00' for an essay (or essays) on the result of some specific clinical or laboratory research in Urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deem none of the offerings worthy, no award will be made. Competitors shall be limited to Residents in Urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years.

Essays shall be in the hands of the Secretary, Dr Clyde L Deming, 789 Howard Avenue, New Haven, Conn, on or before April 1, 1942

PERIPHERAL ARTERIOSCLEROSIS

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A REINTERPRETATION of morphologic changes in sclerotic vessels of the coronary tree substantially altering the concepts of the mechanism of coronary occlusion stimulated our study in peripheral vascular arteriosclerosis. Pat-
terson,^{1, 2} Wartman,³ Winternitz, Thomas and Le Compte,⁴ Leary,⁵ and Horn
and Finklestein⁶ showed that hemorrhage into the intimal plaque in the
coronary artery was a significant etiologic factor in occlusion of the lumen
occurring as the most frequent of all precipitating events. Previous to Pat-
terson's work in 1936, intimal hemorrhage had been noted, but its clinico-
pathologic relationships were overlooked.^{7, 21, 22} The cause of peripheral vas-
cular occlusion, exclusive of embolus, was thought to be either the gradual
compromise of the lumen by an encroaching plaque or the thrombus formation
upon a fatty or hyperplastic plaque in that portion of the vascular tree where
arteriosclerotic changes were so frequent that reduced blood velocity and
ischemic endothelium set the stage for platelet and fibrin deposition.⁴⁸

We surveyed the arteriosclerotic peripheral vessels found in 74 amputated
lower extremities to determine the series of events within the vessel wall
culminating in occlusion. The specimens amputated because of peripheral,
uncontrolled gangrene, and collected as routine surgical material over a period
of three years, were examined to determine the frequency of all of the causative
mechanisms of the peripheral vascular occlusion. The material was analyzed
to evaluate the influence, if any, of diabetes mellitus upon the mechanisms of
occlusion in the peripheral vessels. The technic of controlled trypsin digestion
was undertaken to establish the nature of fibrinoid substance and to determine
the state of the stroma within the atheroma. The importance of hemorrhage
within the intima of the arteriosclerotic vessels brought up questions concern-
ing the fate of the subendothelial plaque. These issues will be discussed in
order to demonstrate the orderly events in the vessel wall in peripheral vascular
arteriosclerosis which lead finally to the catastrophic thrombosis.

METHODS AND MATERIAL—Seventy-four lower extremities were received
as surgical specimens after amputation for peripheral gangrene associated
with either diabetes or arteriosclerosis. The vascular tree was removed *en*
masse with a minimum of trauma and immediately fixed in 20 per cent
formalin. The vessels were rapidly decalcified and sectioned in serial fashion.

* Theodore Escherich, Fellow in Pathology

at intervals of 1-3 Mm. Each section was examined macroscopically. Those which presented the gross findings of luminal occlusion were studied histologically. Hematoxylin and eosin were used as the routine stain. Weigert's Elastica, van Gieson and Mallory-Azan connective tissue stains, Bielschowsky's silver impregnation, Sudan III stain for fat on both simple and gelatin frozen-section, the Lepelme preparation for hemoglobin and the iron stain for blood pigment were employed wherever indicated.

Particular attention was paid to that part of the vessel which showed the most recent change. Patent segments of vessels proximal to the level of occlusion were studied to define the mural lesions which subsequently led to thrombosis. Macroscopic diagnosis of the nature of occlusion in each vessel was checked by histologic examination. Microscopic serial sections were made in ten instances to trace mural capillaries to their origin.

Trypsin digestion was used to determine the character of the stroma of the atheroma and to define the fibrinoid substance. This technic, described by Romeis⁸ and modified for our purpose, consisted of placing the deparaffinized microscopic section in a saturated solution of trypsin at the p_H of seven to eight. A small amount of chloroform or toluol was added in order to prevent bacterial growth. The digestion of blood elements and tissue took place in a sequential manner, *i.e.*, serum and nuclear protein, fibrin, blood platelets and the white blood cells were first consumed.⁹ Red blood cells were the most resistant of all the blood elements. The interfibrillar ground substance disappeared before young connective tissue fibers. Completely necrotic collagen was somewhat more resistant than fibrin, but was digested before partially degenerated connective tissue. Adult healthy collagen remained after all other protein had been consumed, but eventually it too disappeared.

Pathogenesis of Intimal Changes which Lead to Occlusion—For the purpose of our discussion the arteriosclerotic process in the peripheral artery shall be divided into two pathogenetic phases, (1) the etiologic insult, and (2) the reparative reaction to the damage.

The nature of the initial insult to the vessel wall has still been undetermined. The influence of the high fat diets of Saltykow,¹⁰ Anitschkow,¹¹ and Leary¹² in producing experimental atherosclerosis must be reexamined to determine their significance in view of the work of Aschoff¹³ reviving the wear and tear concept of Virchow to show that the first detectable finding in the vessel is not a cholesterol impregnation in an otherwise healthy area, as the experimental atheromatoses in the rabbit would indicate but rather that the primary lesion of arteriosclerosis occurs as a change in the interfibrillary ground substance. Aschoff has emphasized that the ground substance is a complicated colloidal-gel system in constant fluid equilibrium with itself. Whether this change represents physiologic senescence of connective tissue or the first step in arteriosclerosis is difficult to determine, and for our purposes is of no immediate import. The foregoing facts have been demonstrated by Lange,¹⁶ and Leary¹⁴ in young individuals succumbing to unrelated disease processes. In the aortas of the youths, barely visible, slightly raised, tan

streaks are found, running longitudinally on the posterior wall between the intercostal vessels, transversely in the sinuses of Valsalva and about the occluded ductus arteriosus. Histologically, the first change to be noticed in these "endothelial blisters," described in detail by Zinserling,¹⁷ is a separation of the subendothelial structure of the intima by a finely granular, edematous pale material which does not take the stains for fat.¹⁴ The substance is acellular and structureless. Aschoff has interpreted this change as an alteration of hydration of the colloidal-gel. Lange,¹⁸ and Leary¹⁴ termed the state one of "mucoid degeneration." Duff¹⁵ noted a similar state in the media.

The nature and morphogenesis of the fat deposition has still remained unsolved.^{16, 17} Anitschkow and the Russian school¹¹ definitely demonstrated by the fat feeding experiments in the rabbit that the lipids diffuse from the blood stream through intact endothelium toward the media. Winternitz⁴ has suggested that the cholesterol is gathered from extravasated blood elements and serum infiltration, the so-called "exudative" or first phase in the pathogenesis of arteriosclerosis. As yet the significance of fat infiltration as to origin and fate in arteriosclerosis has not been unveiled. Its relation to the high fat dietary habit of man has been inconclusive despite Snapper's¹⁸ remarks that in West China, where the habitual diet is low in fat, coronary occlusion has never been observed.

The second phase of the arteriosclerotic process is essentially the reparative response to the damage initiating in the ground substance and the cholesterol deposition.⁶ The repair consists of capillary sprouting, fibroblastic proliferation and phagocytosis of the lipids, a typical nonspecific body reaction forming in the wall of the vessel a cellular, vascularized plaque of granulation tissue. The subsequent course depends upon the degree of capillary response which Leary¹⁹ has demonstrated to be proportionate to the age of the patient. If the vascularization of the newly formed plaque is nutritiously adequate, the fat is entirely resorbed and collagen is laid down to form a hyperplastic scar. The fibroblasts growing into the damaged area roughly perpendicular to the long axis of the vessel lay down collagen in a pattern concentric with the lumen. As the connective tissue contracts, most of the capillary sprouts are cut off and the final picture of an avascular fibrous plaque manifests itself.

While the fibrotic plaque represents the most advantageous end-stage, another course of events ensues when the capillary proliferation is less pronounced. A state of tissue starvation results and eventually the entire area undergoes ischemic necrosis. In the well vascularized plaque of thriving granulation tissue, there is excessive fibroblastic activity and a minimum of free extracellular fat. In a poorly vascularized plaque, there is slight fibroblastic activity and excessive amounts of extracellular but noncrystallized fat deposited in a fine fibrillary framework. In a totally inadequately vascularized plaque, the fibroblasts are absent. Fat has crystallized on a necrotic structureless afibrillary stroma.¹⁹ This final state represents the mature atheromatous abscess, an end-stage of atherosclerosis much less advantageous than the fibrotic plaque.

Further expression of the necrosis in the mature atheroma is the formation of calcium salts of the fats. The calcium salts appear first as microscopic granules scattered throughout the atheroma, later they coalesce to form large calcium plaques.

The formation of bone in the intima parallels the deposition of calcium. This type of osteogenesis is not the same as that which is found in the long bones of the body where osteoblasts and a predisposing cartilaginous structure are of primary importance. Similar bone formation has been described by Allen²⁰ in breast tumors, where there was no preexisting cartilage. Allen's statement that heterotopic ossification represents a differentiation in no way corresponding to the "concept of preformed cellular endowments" but rather is a manifestation of the dictates of environment, appears to apply to the human arterial wall, where cartilage is never seen, and osteoblasts are conspicuously absent. While capillaries are characteristically not frequent about areas of calcification, they are much more evident about the sites of secondary ossification, particularly where the marrow is differentiated. What the significance is of this observation, noted also by Horn and Finkelstein,⁶ is as yet unknown. In any event, intimal petrification becomes another end-point in arteriosclerosis, representing a much less advantageous result of the reparative processes than the fibrotic plaque.

In the mature atheroma, it has been emphasized that the paucity of capillarization is the factor responsible for the end-stage of atheronecrosis. However, close inspection of the atheromatous abscess reveals that whatever vascular channels do exist are found at the periphery of the lesion and that the center of the atheroma only is devoid of capillaries. The integrity of the delicate wall of the capillary maintaining itself against the pressure of the blood stream depends upon the surrounding extravascular stroma. When the stroma undergoes necrosis, the support of the capillary disappears, rhexis of the wall follows, and a flooding of blood elements ensues into the atheromatous abscess. Our material showed that the athero-hematoma was as frequent in patent vessels as in the freshly occluded portion of the arterial tree. Factors, other than stromal necrosis, have been proposed in playing a rôle in the capillary rupture. Boyd⁷ believes that the athero-hematoma represents an inflammatory reaction. Paterson¹ suggests that the rupture of the capillary is related to the variations in the pressure of the parent vessel from which the intimal capillary is derived. In the capillary of the peripheral vascular bed the tension of the blood flow is practically independent of the pressures of the large arteries because of the friction losses dissipated within the extensive peripheral bed. *Per contra*, the mural capillary, situated anatomically only a short distance from the main arterial lumen and in immediate communication with it, is completely dependent upon the changes in the blood pressure therein.

The location of the hemorrhagic atheroma within the intima is the etiologic important factor which governs the course of subsequent happenings. The occurrence of a small hemorrhage in a plaque which does not encroach upon the lumen eventuates only in scar tissue. The event of a small hemorrhage

in a plaque which already has severely compromised the lumen or of a massive hemorrhage in a mildly sclerotic vessel unaccompanied by endothelial destruction results in occlusion without thrombosis (Fig 1) Here the swelling of the plaque assumes such proportions that the occlusion is entirely mechanical. Hemorrhage immediately beneath the endothelium in a necrotic fatty plaque is followed by luminal thrombosis in the majority of instances of recent occlusion (Fig 2) Microscopic serial sections of athero-hematomata located beneath the fresh thrombus reveals that rupture of the plaque into the lumen is not always necessary for thrombus formation. The injurious effect of sudden

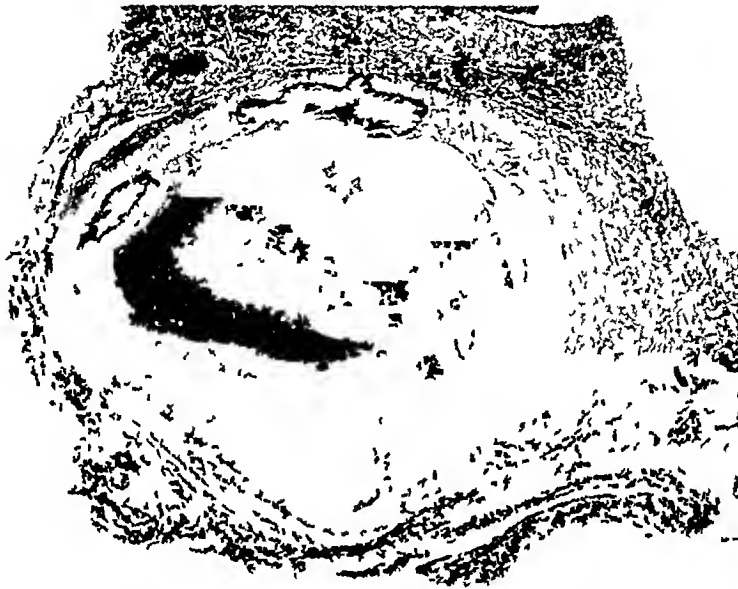


FIG 1—Massive hemorrhage into intimal fatty plaque, with compression occlusion of lumen (X18)

swelling of the atheroma under the endothelium is sufficient to set the stage for platelet and fibrin deposition.²³

The fibrotic plaque, described previously as an advantageous stage of healing, in time may arrive at a less desirable end. As the scar tissue contracts capillaries are choked off until ischemic changes occur. The collagen undergoes necrosis to form a completely avascular atheroma. The morphogenesis of necrotic stroma, fat deposition and subsequent calcification is in every way identical with primary atheromatous abscess. If this degeneration occurs close to the endothelium, the possibility of occlusion by similar mechanisms to those of the primary fatty plaque are evident. Occasionally the atheroma without the insult of hemorrhage precipitates thrombosis. If the enlarging fatty mass situated in the subendothelial stroma causes necrosis of the endothelium, thrombosis results upon the ragged overlying ulcer.⁴⁸ This mechanism of occlusion was particularly frequent in the specimens of arteriosclerotic thrombosis of the aorta which, relative to our subject of the mechanism of occlusions in the vascular tree, were also examined. In the peripheral artery, thrombosis upon the atheromatous ulcer was uncommon.

PERIPHERAL ARTERIOSCLEROSIS

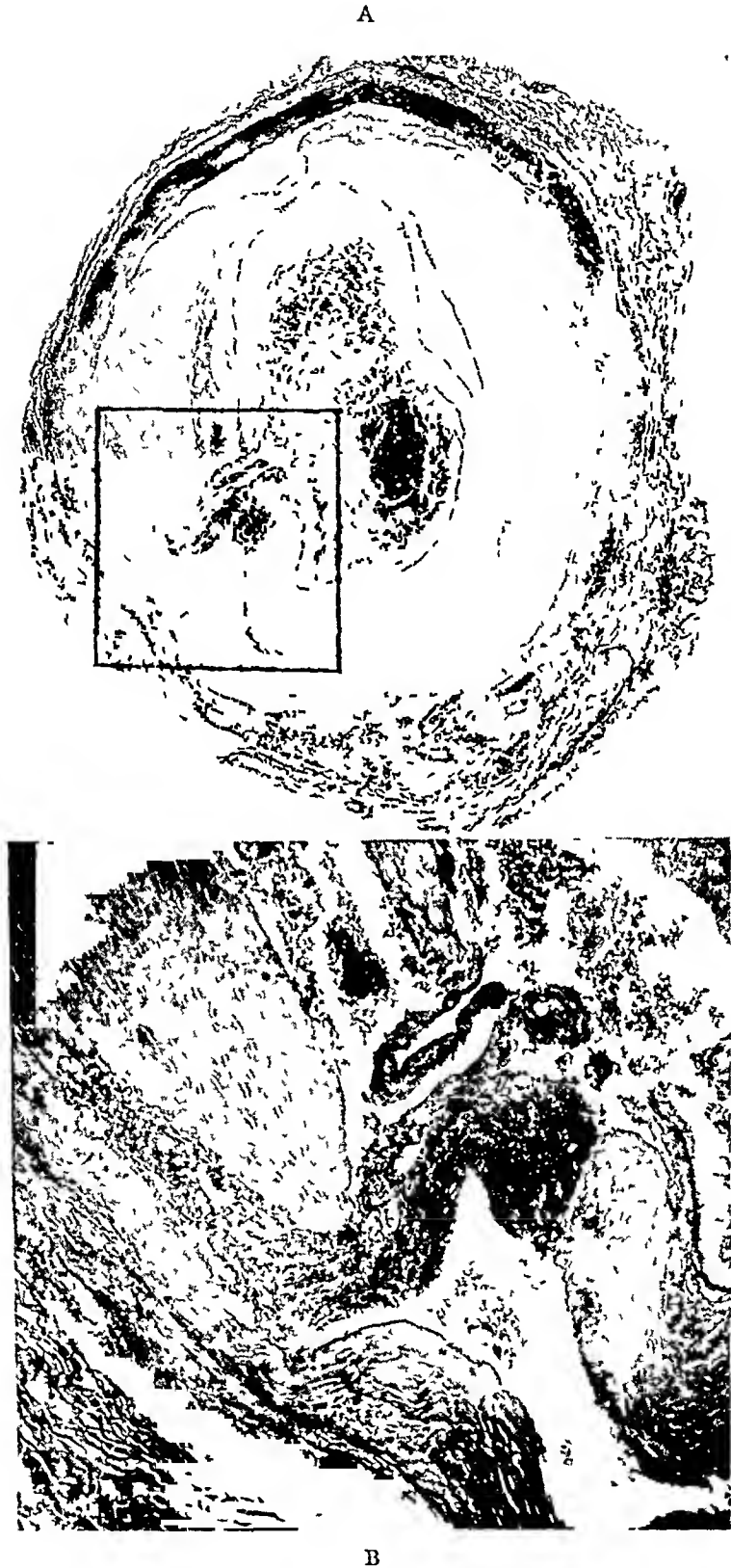


FIG 2 — (A) Hemorrhage into intimal fatty plaque, with endothelial destruction and luminal thrombus ($\times 28$) (B) Higher power photomicrograph of area outlined in Fig 3a ($\times 100$)

The fibrotic plaque undergoes ischemic changes at times in another direction. The connective tissue is converted into a state of degenerated collagen, assuming the properties of "fibrinoid" substance. If this reaction takes place immediately beneath the endothelium, associated ischemic changes of the endothelium lead to thrombus deposition.

Regardless of the nature of the arterial occlusion peripheral gangrene always mirrors a failure of the arterial perfusion. Since anastomotic arterial shunts in the lower extremity are extremely numerous even in the healthy state, massive damage to the arterial tree of the leg has to be inflicted before gangrene ensues. In all of our specimens, at least two out of the three large arteries of the leg are either occluded or severely encroached upon. This pathologic picture corroborates Veal's²⁴ arteriographic findings in intermittent claudication in legs of competent perfusion, one vessel is occluded in 50 per cent of cases, marked narrowing without obstruction is found in 13 per cent, and the remainder of the series shows many obliterated finer branches with patent large arteries. Likewise, in our specimens, multiple focal occlusions throughout the vascular tree were the rule. The usual picture was to find old fibrotic luminal occlusions in the distal segments of arteries while proximally either a recent thrombus or some other type of acute occlusion was manifest. In 15 specimens of this series, the only type of occlusion to be noted was fibrotic scar tissue. No recent thrombus was found. This situation occurred particularly in the limbs amputated at the level of the lower third of the leg. In the same group, specimens of reamputation also occurred. Our subsequent statistics on the categories of vascular occlusion are affected by these facts. The group of acute closures is conceivably too low, the frequency of old healed thrombi too great because the presence of an acute vascular accident proximal to the level of amputation was not ruled out. The fact that the surgical stump healed at a level below which no recent occlusion was found was of no import in the exclusion of a fresh luminal thrombus above the site of amputation.

Types of Vascular Occlusion—By analysis of our material there was established definite morphologic evidence leading to peripheral vascular occlusion. The appended grouping and Table I comprised the categories of lesions within the arterial tree which reduced perfusion to such a level that peripheral gangrene followed.

- Group I Thrombosis secondary to hemorrhage
- Group II Thrombosis upon a plaque
- Group III Massive hematoma of the wall
- Group IV Arteriosclerosis with
 - (1) Severe luminal encroachment
 - (2) Narrowing and thrombosis
 - (3) Mural hemorrhage
 - (4) Hemorrhage and thrombosis
- Group V Granulation tissue

We were guided by several principles in determining into which category each of our specimens belonged. The most recent proximal occluding lesion was always regarded as the precipitating cause of the peripheral gangrene. The presence of extensive arteriosclerosis with luminal encroachment or old organized distal occlusions was relegated to secondary importance in the

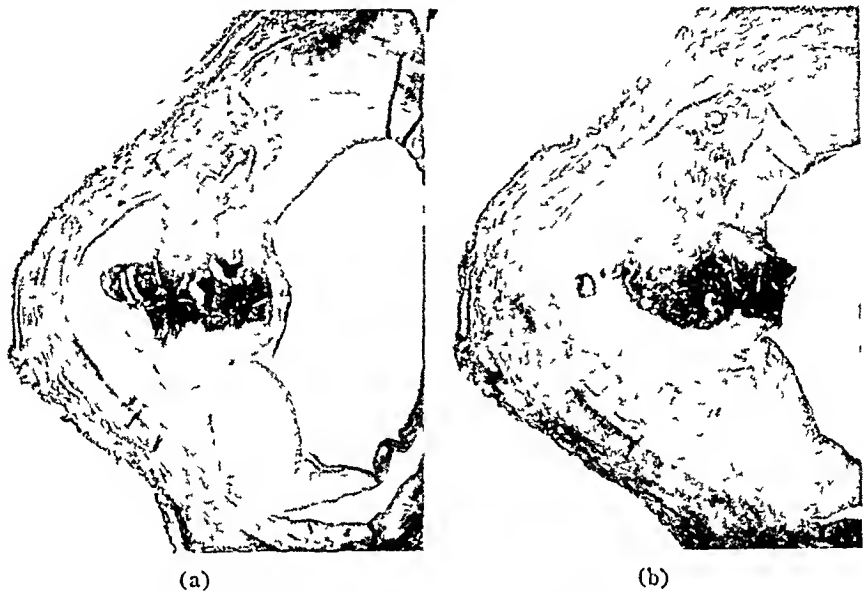


FIG. 3 —(a) Intact atheromatous abscess in intimal hyperplastic plaque, with small parietal overlying thrombus ($\times 17$). (b) Same lesion as in Fig. 4a at level of ulceration into lumen, with seepage of blood elements into subendothelial portions of plaque ($\times 15$).

presence of recent proximal thrombosis. The latter was the imminent factor in the process of the peripheral gangrene, before this, the impairment of circulation by previous insults was not severe enough to cause necrosis. When no acute lesion was found, old fibrotic organized occlusions were considered of greater import than severe arteriosclerosis with narrowing of the lumen. In Group IV, where the primary occluding mechanism was the excessive arterio-

TABLE I
MECHANISMS OF PERIPHERAL VASCULAR OCCLUSION

Group	No. of Specimens	Percentage
I Thrombosis secondary to hemorrhage	36	49%
II Thrombosis upon a plaque	5	7%
III Massive hematoma of the wall	1	1%
IV 1 Arteriosclerosis with severe luminal encroachment	11	15%
2 Arteriosclerosis with narrowing and thrombosis	1	1%
3 Arteriosclerosis with mural hemorrhage	4	5%
4 Arteriosclerosis with hemorrhage and thrombosis	1	1%
V Granulation tissue	15	20%
Total number of specimens	74	

sclerotic proliferation with great reduction of luminal size, the occurrence of acute mural hemorrhage and/or fresh thrombosis in the pin point lumen was regarded as a mere coincidental event.

GROUP I—*Occlusion by Thrombosis with Intimal Hemorrhage*—Thrombosis upon intimal athero-hematoma constituted the nature of occlusion of the largest group of our cases. The lesion was found in 36 (49 per cent) specimens. The thrombus varied from the typical picture of layered platelet and

fibrin deposition with the other formed blood elements caught in the interstices to the more organized states of capillary sprouting, cellular infiltration and fibroblastic proliferation. Beneath the thrombus the endothelium was either disrupted or intact. If the athero-hematoma occurred immediately under the endothelium, an actual dehiscence of the latter resulted, the hemorrhages of the mural plaque broke into the blood stream, and thrombosis eventuated on the necrotic and hemorrhagic mural ulcer (Fig. 2). However, if the hemorrhage took place deep in the intima, the endothelium was found intact despite thrombosis. This fact was established only after serial sections were made through the entire length of the atheroma. In these specimens, the swelling of the atheroma by the blood elements seemed to have damaged the endothelium sufficiently to precipitate thrombus formation.²³

In order to determine the source of the intimal hemorrhage, study of the atheromatous abscess was pertinent. In the intact early (immature) atheroma, the stroma was fibrillary, relatively healthy connective tissue. Large amounts of uncrystallized lipids existed in the interstices. Many capillaries, frequently dilated, coursed through the lesion. The framework had the staining characteristics of healthy collagen. At the periphery, the fibrillary stroma gradually blended into the surrounding dense connective tissue.

In the advanced (mature) atheroma the fibrillary framework was replaced by structureless, smudgy acellular mass. Cholesterol crystals were deposited in acicular fashion. The connective tissue stains revealed that the collagenous stroma was in a state of advanced necrosis.^{5, 12} Sudan III shows an intensive accumulation of fat in noncrystalline as in the crystalline state. Trypsin rapidly digested this necrotic mass leaving behind the encircling healthy capsule. At the periphery of the atheroma there was a characteristic separation of collagen fibers to fray as individual strands and dangle freely in the atheroma. Though relatively infrequent, capillaries extended from the capsule of the lesion into the necrotic plaque. Whereas the integrity of the capillary wall depended for support on the surrounding stroma, the necrotic state of the latter assumed singular import in the rhexis of the delicate walls of the former. Thus, the mechanism of mural athero-hematoma became evident.

GROUP II—*Occlusion by Thrombosis without Intimal Hemorrhage*—Thrombosis upon an intimal plaque without hematoma was found five times (seven per cent) in our series. In past years, this mechanism of occlusion had erroneously been believed to be most frequent.⁶

Many have observed that it was impossible to produce experimental thrombosis of either artery or vein without damaging the endothelium.^{23, 25} In arteriosclerosis the subendothelial connective tissue mirrored the health of the endothelium. In each instance of thrombosis upon an intimal plaque there was extensive degenerative lesions beneath the thrombus formation. In one case, where an atheromatous abscess was found immediately under the endothelium, the necrosis of the stroma so compromised the endothelium that rhexis resulted. In Figure 3 a, a parietal thrombus has formed over the mural necrotic fatty avascular plaque. In Figure 3 b, the plaque has broken

through the endothelium, fibrin and serum have infiltrated into the subendothelial zone which assumes an azure character distinct from the brighter red necrotic stroma deeper in the lesion. Trypsin digested the fibrin and serum proteins to leave the uniform homogeneous necrotic framework of the atheroma.

The other specimens which presented thrombosis upon plaques without intimal hemorrhage manifested a different status of degeneration in the underlying arteriosclerosis. Beneath the endothelium the degenerative "fibrinoid" change was noted in the sclerotic plaque. This degeneration, first described by Neumann,²⁶ appeared homogeneous, smudgy, acellular and intensely red in the routine hematoxylin and eosin preparation. Tinctorially, fibrinoid substance duplicated all the properties of fibrin to such an extent that some workers^{22, 27, 28, 29} believed both substances to be identical. Others^{30, 31} postulated that the fibrinoid appearance of collagen was due to a splitting of the connective tissue into its component fibrils, with seepage of fibrin into the interfibrillar spaces. Trypsin digestion definitely differentiated fibrinoid substance from fibrin. In controlled digestion the fibrin and cellular elements of the thrombus disappeared while the fibrinoid matter remained untouched. Connective tissue stains revealed the same separation, fraying and dangling of healthy collagen fibers at the edge of this substance that was found at the periphery of the atheroma. Moreover, trypsin digestion differentiated fibrinoid substance from the necrotic stroma of the atheroma, for after exercising extreme care in controlling the digestion we found that the atheromatous framework was consumed before the fibrinoid material was touched. The fibrinoid substance, in turn, was digested before healthy collagen was altered. With this differential digestion, we separated the fibrinoid change from true fibrin, and entertained the thought the fibrinoid change was an alteration in the state of collagen. A more detailed account of this phase of arteriosclerosis will be dealt with in a forthcoming publication.

GROUP III—*Occlusion by Plaque due to Intimal Hemorrhage*—The encroachment upon the lumen by intimal athero-hematoma to such a degree that circulatory insufficiency resulted comprised a small but extremely significant group of our specimens (Fig 1). In one instance, this lesion accounted for the closure of the popliteal artery and was the significant factor in producing the peripheral gangrene. In three other instances massive athero-hematoma were also responsible for occlusion, but since, at more proximal levels, thrombus formation within the lumen was associated with the same catastrophe, these specimens were classified elsewhere. In a host of other sections recent mural athero-hematoma without encroachment of the lumen were found. The common occurrence of the mural hemorrhage in the patent portion of the arterial tree, as well as in the more distal occluded areas, tended to establish the mural lesion as a forerunner of thrombosis (Fig 4). If mural hemorrhage occurred without luminal obstruction, no decrease of circulatory perfusion resulted. In the instances where intimal athero-hematoma occurred without endothelial compromise or rupture, occlusion resulted when encroachment upon the lumen was complete. The pathogenetic import of mural hem-

orrhage within the larger group in which arterial thrombosis followed the athero-hematoma became apparent from the study of this smaller group of specimens. The thrombus occurred only as a sequela of the hemorrhage chronologically happening later in the processes of arterial occlusion as a catastrophic end-stage.

GROUP IV—*Occlusion by Extensive Arteriosclerosis*—Severe arteriosclerosis, morphologically delineated by all of the changes noted in the advanced state,^{32, 33} and functionally associated with extreme reduction in luminal size, was found in 17 (23 per cent) specimens. In 11 instances, the patent lumen



FIG. 4.—Hemorrhage in a massive atheromatous abscess occurring as an incidental finding in the femoral artery proximal to occlusion of the popliteal artery by thrombosis which was secondary to mural athero hematoma.

was traced throughout all of the sections. Blumgart, Schlesinger and Zoll,³⁴ and Friedberg and Horn³⁶ renewed interest in a comparable condition within the heart, the state of coronary insufficiency or failure. They found that the incompetency of myocardial perfusion associated with the severe arteriosclerosis and luminal narrowing resulted in subendocardial myomalacia, a comparable condition to the distal phalangeal gangrene characterizing our specimens in which severe arteriosclerosis occurred. Whereas it was beyond the scope of this discussion to enumerate the dynamic factors brought into play in the precipitation of the gangrene, this subject has been discussed in detail by Friedberg and Horn³⁶ in its relationship to the coronary tree, and by Hines and Barker³⁵ in the peripheral arteries.

Coincidental to the extensive arteriosclerosis, a thrombotic obliteration within a pin point-sized lumen was found in one instance. Fresh subendothelial hemorrhage occurring five times was the precursor of a luminal thrombosis in one specimen.

It must be emphasized that despite the fact that the arterial tree possessed no actual occlusion in the 11 specimens of arteriosclerosis with narrowing of

the lumen we realized that a thrombotic process might have been located above the level of amputation. The fact that the stumps subsequently healed did not fully rule out this possibility.

GROUP V—Occlusion by Granulation Tissue—In 15 (20 per cent) specimens the lumen was completely obliterated by fibrotic scar tissue. It was impossible, microscopically, to differentiate the vascular channels as to whether

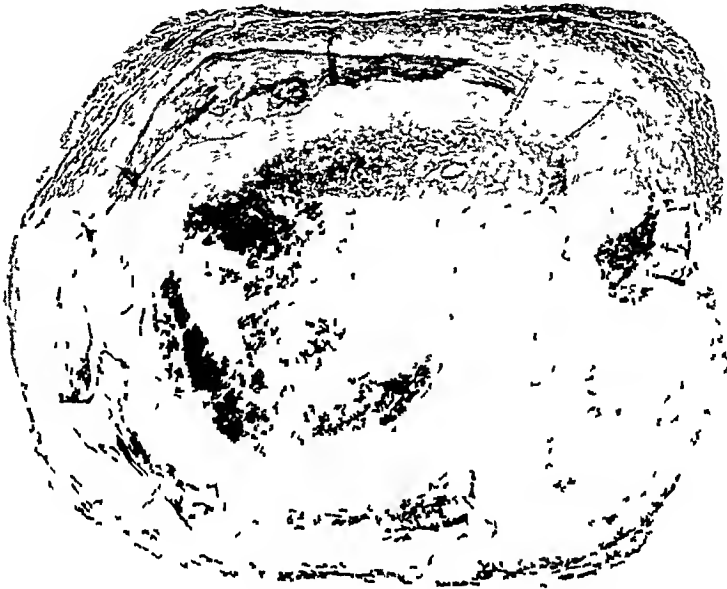


FIG. 5—Recent hemorrhage into old granulation tissue occlusion (×29)

they represented recanalizing capillaries or residua of the original lumen. Moreover, it was impossible to determine through what mechanism the scar obliterating the lumen originated and what end-stage it represented.^{4, 6} The collagen pattern was unrevealing. The presence of iron pigment was of no help, for both intimal hematoma and luminal thrombus leave the same residue. The presence of subendothelial elastic fibers was of little aid. They were not infrequently observed about recanalized channels as well as the true lumen. Horn and Finklestein,⁶ and von Glahn³⁷ noted a similarly confusing state in vessels of the coronary tree.

In the old fibrotic occluded vessel, a frequent finding was that of secondary atheromatous abscess and fresh hemorrhage with the luminal scar (Fig. 5). When a state of ischemia resulted within the organizing thrombosis, the atheroma was formed. As it underwent necrosis, capillary rhexis and hemorrhage resulted.

Diabetes—No specific effects of diabetes mellitus were noted in any specimen upon the pathologic events within the arterial tree resulting in peripheral gangrene. We were unable to distinguish any unique morbid features in the diabetic vessels. Eliason and Wright⁴⁹ found that 55 per cent of the cases of senile gangrene of the lower extremities were diabetic. In our series of 74 specimens, 35 (44 per cent) were diabetic. In Table II, we subdivided the

mechanisms of arterial occlusion into diabetic and nondiabetic categories. Outside of the fact that all five instances of thrombosis upon a plaque fell into the nondiabetic group, no significant difference was evident.

TABLE II
MECHANISMS OF ARTERIAL OCCLUSION IN DIABETIC AND NONDIABETIC CATEGORIES

	Thrombosis upon Hemorrhage	Thrombosis upon Plaque	Mural Hematoma	Severe Arteriosclerosis	Granulation Tissue
Diabetic	19	0	1	7	8
Nondiabetic	17	5	0	10	7

Mural Vascular Tree—The vascular supply to the arterial tree brought up many questions which have yet been unanswered. In the healthy vessel, the presence of mural capillarization has remained a matter of dispute. In the intima, capillaries have not been found. Although Winternitz and his coworkers^{4, 38} demonstrated an arborizing network in the intima of the aorta of a healthy cow by subendothelial perfusion of India ink at the tremendously high pressures of 500 to 1,000 Mm. of mercury, this has never been duplicated in normal human vessels. These capillaries were demonstrated in the intima of the bovine aorta in order to establish their possible rôle in arteriosclerosis. Since Goldblatt³⁹ emphasized that arteriosclerosis in the cow's aorta was never found to involve the intima but was limited to the media, the pathogenetic relationship of intimal capillarization to bovine arteriosclerosis was not pertinent. The course of capillaries has been followed from their origin in the vasa vasorum through the outer zone of the media in human vessels unaffected by arteriosclerosis⁴⁰. An occasional capillary traversed the middle portion of the medial coat, but none were seen in the inner zone⁴¹. In the aorta of the horse and the dog, Woodruff⁴² established a medial vascularization by injection of India ink and gelatin into the vasa vasorum. Gross and his coworkers,⁴³ and Horn and Finkelstein⁶ denied the presence of any capillaries in the media of normal coronary arteries. It was our impression that if they did exist in healthy peripheral vessels they were infrequent. The nutrition of the wall of the normal vessel, because of the absence of vascularization, must be derived largely from the blood stream⁴⁴. Anitschkow¹¹ showed evidence for this hypothesis by intravital trypan blue injection, in which the dye was seen to diffuse through the intact endothelium into the wall of the vessel.

In contradistinction to the absence of intimal vascularization in healthy arteries the presence of intimal blood supply in arteriosclerotic vessels has been well-recognized^{4, 45, 46}. The origin of the mural capillary has long been a subject of controversy. Some investigators^{37, 43, 47} claimed the vasa vasorum to be the more common source, while others^{1, 2, 3, 12} felt that they rose chiefly from the main lumen of the vessel. By serial survey of ten representative sections we traced intimal capillaries back to the lumen of the vessel as well as to the vasa vasorum. From both sources there arose an intercommunicating anastomatic network of vascular channels. The distribution of the capillary network of the intima was particularly noted. It was most abundant in young

plaques where fresh organization occurred. It was least evident in areas of complete fibrosis. As the paths of the capillaries were traced through the media and internal elastic membrane, they were found to enter a relatively fresh area of granulation tissue. As the capillary approached a zone of dense fibrosis, it either skirted the area, terminated abruptly, or occasionally remained as a ghost-lumen filled with either a hyalinized or calcified thrombus. This gave the impression that the contraction of the scar had choked-off its own blood supply.

In the atheromatous abscess, capillaries were inconspicuous except in the periphery of the lesion. As they penetrated towards the necrotic center, necrosis occurred in their delicate thin walls. The nuclei and cellular outlines disappeared and were replaced by an eosinophilic granular structureless substance. Rupture resulted through the necrotic wall allowing extravasation of the blood elements into the atheroma.

In the vessels in which complete occlusion occurred, mural capillaries might assume a function other than that of nutrition. It was conceivable that they might constitute an attempt at intravascular collateral circulation. Winternitz and his coworkers³⁸ indicated the establishment of such a collateral channel by perfusion and injection technic. We attacked the problem by studying the stage of the thrombus and comparing the number of capillaries found therein with the number found within the wall of the main vessel. The mural circulation showed a rough relationship to the stage of occlusion. Old fibrotic, avascular occlusions showed an abundant mural vascularity, an attempt has been made within the wall of the vessel to shunt the blood flow around the occluded portion. Mural capillaries were less abundant in vessels which revealed extensive recanalization of the occluding thrombus, the recanalized channels within the thrombus assumed the burden of the circulation (Fig. 5). Roughly, an inverse ratio existed in the degree of capillarization between the luminal occlusion and the mural collateral response.

SUMMARY

(1) In 74 cases of gangrene of the lower extremity necessitating amputation, the vascular tree was studied in order to establish the pathogenetic events leading to occlusion and to classify the types of arterial occlusion. The rôle of mural hemorrhage was emphasized as the most frequent factor precipitating acute luminal thrombosis.

(2) A study of the atheroma, its capillarization, and the state of its stroma was reviewed to establish the fact that intimal hemorrhage was secondary to rhexis of the vascular channels traversing the necrotic atheroma.

(3) All types of occluding mechanisms were discussed in order to determine the importance of each. Arteriosclerosis with severe encroachment of the lumen was second in frequency to thrombosis upon athero-hematoma.

(4) A means of differentiating the fibrinoid substance from fibrin by trypsin digestion was described. A relationship between the fibrinoid substance

and partially degenerated collagen based on the results of trypsin digestion was entertained

(5) Intimal and medial capillarization in arteriosclerotic vessels were traced to both the lumen and the vasa vasorum. Their reparative significance in the process of arteriosclerosis and their anastomotic importance in arterial occlusion were discussed

(6) No difference was noted between the arteriosclerotic findings of the diabetic from the nondiabetic specimens

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THE TREATMENT OF SEVERE STAPHYLOCOCCAL INFECTION WITH SPECIFIC TYPE-A ANTIBACTERIAL SERUM

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ANALYSIS OF STATISTICS from various sources, both in this country and abroad, reveals that staphylococcal septicemia is an infection accompanied by high mortality. While the fatality rate varies from 60 to 95 per cent in the different studies recorded, the average must be accepted as 75 to 80 per cent. Despite numerous expedients introduced in the past to improve the statistics, it must be admitted that they have failed in their purpose. Nonspecific measures such as surgical drainage and supportive treatment, undoubtedly of value, are nevertheless insufficient in altering to any marked degree the number of individuals succumbing to this form of septicemia. The recent studies reported by Julianelle^{1, 2, 3} on the classification of staphylococcus, and culminating in an experimental, therapeutic serum,⁴ suggested the possibility that staphylococcal septicemia might be controlled by the administration of antibodies directed against the carbohydrate elaborated by the virulent (*i.e.*, for man) organisms. In his preliminary note, Julianelle⁴ considered the data then available on treatment as inconclusive but encouraging. Eager to determine the therapeutic effectiveness of the antiserum, hereinafter designated as Type-A, arrangements were made with the Lederle Laboratories, of Pearl River, N. Y., to furnish serum for an experimental study in this hospital. The arrangements were made with Doctor Julianelle's consent and approval. The study has continued for about two years, and in the interval, 18 patients with verified staphylococcal septicemia, one with osteomyelitis and transient bacteremia, and three with pneumonia without positive blood cultures, have been treated with the serum.

Experimental—The patients utilized in this study were not selected in any way. Regardless of age, duration of infection, clinical complications, or prognosis, they were accepted for serum therapy on the basis of severe infection, preferably with septicemia. Consequently, a broad variety of staphylococcal infections are represented in the present series. The organisms isolated from the patients were studied for mannite fermentation and type of carbohydrate. Every strain but one was *aurus*, all fermented mannite,⁵ and all yielded, on acid extraction,² the Type-A carbohydrate.

Treatment consisted not only of administration of Type-A antiserum but also of whatever supportive care was indicated, and particularly whatever surgical measures appeared to be advisable at the time. Most of the patients had been under treatment with sulfonamide drugs previous to administration of serum, and in many instances this caused a more prolonged delay in

serum treatment than was desirable. That the sulfonamides had not been effective, however, was the judgment of the physician in charge, and, in fact, a paper now in press⁶ suggests these compounds leave much to be desired in their effect on severe staphylococcal infection. In most of the cases in this study the drugs were discontinued with serum therapy, in a few, however, the drugs were given simultaneously in spite of our order that they be withdrawn. Because of the number dying, however, it may be that the drug was not of great importance in the recovery.

It may serve best the purposes of this communication if the complete data are consolidated in the form of tables, containing the more important details regarding clinical history and treatment of each individual. The only division of patients to be made is that based on ultimate survival or death. While no comment is made in the protocols concerning blood cultures, it may be well to say that each patient had repeated cultures, for the most part both in broth and in agar, with measured quantities of blood to determine the number of staphylococci per cubic centimeter. Septicemia was determined by repeated growth of staphylococci from the blood and by the colony count. On this basis, it can be said that except for three of the five patients with pneumonia, septicemia was established in every patient but one, and in that one the evidence suggests merely a transient bacteremia (Patient I A, Table I). Supportive treatment also has been omitted from the tables since this varied from individual to individual and included whatever was regarded as an adjuvant to the patient's welfare.

ANALYSIS OF PATIENTS SURVIVING INFECTION

The data dealing with recoveries will be found in Table I.

It will be seen that ten patients treated with serum eventually survived the infection. The group consists of five males and five females, with ages varying from 20 months to 43 years. In four of the patients, the septicemia started by way of osteomyelitis, one of whom was further complicated by clinically recognizable myocarditis, subsequently confirmed by electrocardiographic studies. In patient S S, with osteomyelitis of the left femur, serum treatment was delayed until the thirty-first day of illness and was administered by the intravenous (132 cc) and intramuscular (30 cc) routes. In addition to supportive treatment, it was found necessary to incise over the trochanter and to drill openings into the femur where necrosis was found. This resulted in adequate drainage. In patient J T, with osteomyelitis of the right foot, ulna, scapula and left fibula, complicated by myocarditis, surgical drainage was performed at each of these foci as well as four metastatic, subcutaneous abscesses. Serum treatment began on the tenth day of illness, and consisted of three daily administrations of serum of 60 cc, each given intravenously. In patient T N, there was an abscess of the face, parotid gland, and left hand, as well as an osteomyelitis of the right foot. After removal of a splinter in the left hand which may or may not have initiated the original infection, incisions were made over the left hand, right foot and internal malleolus.

Serum was given both intramuscularly and intravenously over a period of nine days. The later injections of serum were given with difficulty because of increasing sensitivity in the child, and, in fact, serum sickness, in the form of urticaria, subsequently appeared. The fourth case was that of a sailor in the U S Navy, with osteomyelitis of all the bones of the left foot, and yielding a single positive blood culture during the period of observation. Serum therapy was given late in the disease and the indications are that no benefit was derived from this treatment. Surgically, a number of procedures were undertaken with eventual amputation of the left leg.

In four other patients, the infection was predominantly pulmonary. In two, the pneumonic process was primary, although postoperative in one, and in two others the pneumonia was secondary to a surface lesion. No positive blood cultures were obtained in three of these individuals, while in one (Patient W H) several consecutive, positive blood cultures were cultivated, the colony count before treatment in fact reaching as high as 145 colonies per cc of blood. In patient R R, the pneumonia appearing in the left upper lobe was secondary to a boil on the left elbow, and was rapidly followed by empyema. In this case, it is probable that despite the negative blood cultures, extension of the infection from the original focus to the lung may have been by way of the blood. Serum was not administered until the twentieth day, and consisted of 60 cc on that day, and 40 cc on the twenty-first and twenty-second day, all given intravenously. The process of recovery was aided by thoracostomy and open drainage on the twenty-first day of disease. Similarly, in Patient W H, the original lesion was a cellulitis of the left hand with an abscess on the back, and subsequently there was a metastatic pneumonia of the left upper lobe. Drainage of the hand and back was accomplished by incisions. Serum was given over a period of seven days, at first intravenously and later intramuscularly. The total amount was 165 cc. The pneumonia appearing in Patient M M followed hemorrhaphy by two days. Recognized early as staphylococcal in etiology, sulfathiazole was given to a total of 54 Gm over seven days, but the infection merely became intensified with the formation of multiple abscesses throughout both lungs. At this time, the prognosis seemed hopeless, but it was, nevertheless, decided to start serum therapy. She received 260 cc intravenously over seven days. The final patient of this group, E E, was a typical example of primary staphylococcal bronchopneumonia confirmed by roentgenologic and sputum studies which yielded pure culture of *Staphylococcus aureus*. Serum treatment was delayed until the eleventh day because the patient was under sulfathiazole therapy (74 Gm during the interval). With no improvement in her general condition, it was decided to give serum instead. Two intravenous injections were given, 60 cc on the eleventh day, and 40 cc on the twelfth day. Twelve hours following the second injection, the temperature fell to normal and remained at that point during the patient's stay in the hospital. The effect of the serum in this group of patients has been particularly striking, the latter two being especially impressive.

TABUL I
SUMMARY OF RECOVERIES FOLLOWING ADMINISTRATION OF TYPH A ANTISERUM

Patient	Color	Sex	Age	Chief Clinical Signs	Day Serum Given	Surgical Care	Total Serum Administered	Skin Test to Carbo hydrates	Serum Sickening
S S	W	M	13 yrs	Osteo lft femur Septicemia	31st	Incision trochanter Drilled holes in femur	162 cc over 9 days	Not done	Urticaria and joint pains
J T	W	F	9 yrs	Osteo rgt foot ulna scapula and lft fibula Myocarditis metastatic skin ab- scesses	10th	Drainage of each osseous focus	180 cc over 3 days	Positive	None
T N	W	M	21 mos	Septicemia Osteo rgt foot Abscess of face parotid, lft hand	6th	Incision int malleolus rgt foot lft hand Showed splinter lft hand	140 cc 1 v and 1 m over 9 days	Positive	Urticaria
I A	W	M	43 yrs	Osteo all bones of lft foot Transient bacteremia	Chronic	Eventual amputation of leg	200 cc 1 v over 5 days	Not done	None
R R	W	M	16 yrs	Boil lft elbow, pneumonia, 1 u 1 Empyema	20th	Resection 3rd rib posteriorly	100 cc 1 v over 3 days	Not done	None
W H	W	M	20 mos	Septicemia not verified Cellulitis lft hand Abscess of back rgt foot Pneumonia 1 u 1	4th	Drainage of lft hand back rgt foot	165 cc 1 v and 1 m over 7 days	Neg ?	None
M M	W	F	42 yrs	Septicemia Postoperative pneumonia	18th	None	260 cc 1 v over 7 days	Positive	Urticaria
E E	W	F	32 yrs	Septicemia not verified Primary bronchopneumonia	11th	None	100 cc 1 v over 2 days	Positive	Urticaria Joint pains
E B	C	F	30 yrs	Septicemia not verified Meningitis	6th	None	80 cc 1 v over 2 days	Not done	None
L D	C	F	41 yrs	Septicemia Meningitis	15th	None	120 cc 1 v over 3 days	Positive	Urticaria

In the final two surviving patients the infection was primarily in the meninges. The one, E B, was a colored woman, who, following an injury, developed all the signs of typical meningitis. Spinal fluid yielded staphylococci on culture and the cell count and protein content were characteristic of purulent meningitis. Serum treatment was started on the sixth day and consisted of two injections. The spinal fluid became sterile several days later. Recovery was complete and the patient was discharged on the sixty-third day following the onset. In the other, L D, a colored female, also, the chief clinical signs were those of meningitis with positive cultures of hemolytic *Staphylococcus aureus* from both spinal fluid and blood. Serum treatment, started on the fifteenth day of illness, consisted of 120 cc given over three days.

It may be well to point out that of the surviving patients, five, or 50 per cent, gave signs of serum sickness. This consisted of urticaria, and in two, joint pains were also present. In each, the condition was mild and responded promptly to symptomatic treatment. Skin tests to the Type-A carbohydrate as suggested by Julianelle⁴ to measure the adequacy of serum treatment were conducted in six of these patients. In five, the test elicited a typical wheal and erythema reaction, while in the sixth patient, the test was negative on the two occasions performed, both before completion of serum treatment.

Twelve patients are recorded in this summary—four males and eight females. Another patient has been omitted from the tabulation because, although serum was given on the eighth and ninth day of infection, which included pericarditis, the physician in charge decided to discontinue serum and give sulfathiazole instead. The patient died 13 days later, so that under the circumstances it cannot be determined what effect the serum actually had or may have had. The ages varied from three weeks to 41 years, and the clinical conditions at the time of first examination were extremely severe, if not critical. Thus, six patients died within 72 hours after first being treated with serum, four, in fact, within 36 hours. In addition, seven patients presented clinically recognizable endocarditis, one pericarditis, and in one even sinus thrombosis was suspected clinically and later confirmed at autopsy. In all but three of the patients dying, postmortem examinations were made so that the ultimate diagnosis could be made with certainty.

In patient B O the chief clinical signs were endocarditis and meningitis. Serum was given intravenously on the ninth, tenth, and eleventh days of illness, 50, 25, and 15 cc respectively. Death occurred on the following day before further serum could be given. Autopsy confirmed the diagnosis of endocarditis (on the mitral valve) and meningitis, and revealed further, hemorrhagic infarcts in the kidneys, spleen, and heart. Patient L C, with osteomyelitis of the left tibia, pneumonia of both lungs, pyonephritis and endocarditis, was placed on serum treatment the sixth day of illness, receiving a total of 480 cc intravenously over nine days. In addition, incisions were made over the periosteum of the tibia and the right ulna disclosed pus in both situations. Considerable supportive treatment was instituted as well.

The colony count ran consistently high, and on the tenth day of treatment the patient expired. Postmortem examination disclosed multiple abscesses of lungs, spleen, and kidneys and a vegetation on the tricuspid valve. Patient T K, with indefinite portal of entry, presented on examination symptoms of endocarditis. Serum was given on the seventh, eighth, and ninth days, 60, 40, and 40 cc, respectively. On the tenth day, death occurred. Autopsy revealed a perforated interventricular septum, perforation and vegetation of the aortic valve, and hemorrhagic infarct of the spleen. In patient J N endocarditis followed postabortal endometritis. Serum was given on the fifteenth, sixteenth, seventeenth, and eighteenth days, 160 cc in all. Death ensued on the eighteenth day. In addition to infection of the uterus and endocarditis, postmortem examination showed the presence of hemorrhagic infarcts of spleen and lungs. Following suprapubic prostatectomy, patient S C developed both pneumonia and endocarditis despite immediate treatment with sulfathiazole and later sulfadiazine. On the sixteenth day, 80 cc of serum were given intravenously, and within 24 hours, the patient died. At autopsy, there was seen a vegetation on the mitral valve and extensive bronchopneumonia. Patient A M was admitted on the third day of illness in a stupor and with definite clinical signs of endocarditis. Serum was given intravenously, 120 cc, and within 24 hours the patient died. Autopsy revealed a vegetation on the mitral valve, a focal abscess on the left ventricle, abscesses of spleen and kidneys and petechial hemorrhages of the gastro-intestinal tract, skin, and conjunctivae.

The final patient in this group, W T, showed early evidence of endocarditis without demonstrable evidence of the portal of entry, although a chronic prostatitis may have been the primary focus. Serum therapy was begun on the eleventh day of disease and was continued for four consecutive days, for a total dosage of 240 cc. The patient died on the fifteenth day of disease. Postmortem examination revealed mitral valvulitis, multiple abscesses of the viscera, prostate, and brain, and petechiae of skin and conjunctivae. The foregoing group of patients, complicated with endocarditis when first seen, was a particularly unfair trial for any treatment. This is at once apparent when it is realized that two of the seven died within 48 hours, and two within 72 hours, thus suggesting, immediately, that the patients were hopeless at the very start. The remaining patients, however, survived four, five, and ten days. The indications are that in endocarditis the prognosis is still hopeless even with the added treatment of specific antiserum.

Another patient presented pericarditis as the chief therapeutic difficulty. Thus, D K had multiple skin abscesses, pneumonia of the right upper lobe, and pericarditis, probably all secondary to a paronychia on the left thumb. Sulfathiazole had been used before serum therapy, without checking the infection. A roentgenogram of the right femur the day before death showed osteomyelitis with extensive necrosis of the bone. Surgical treatment consisted of repeated pericardial taps and pericardotomy, with insertion of drain. From the eleventh to the nineteenth day antiserum was administered intra-

TABLE II
SUMMARY OF SERUM TREATED PATIENTS WITH FATAL STAPHYLOCOCCAL SEPTICEMIA

Patient	Color	Sex	Age	Additional Clinical Signs	Day Serum Given	Surgical Care	Total Serum Administered	Death Following Serum	Autopsy Findings
B O	W	F	23 yrs	Endocarditis	9th	None	90 cc 1 v over 3 days	Within 72 hrs	Menngitis, mitral valvulitis, infarcts kidneys spleen heart G I tract and liver
L C	C	F	11 yrs	Menngitis Osteo lit tibia Pneumonia lit lung Pyonephritis	6th	Incision perosteum lit tibia rgt ulna	480 cc 1 v over 9 days	10 days	Multiple abscesses lungs spleen kidneys, vegetation tricuspid valve
T K	C	F	23 yrs	Endocarditis acute gangrenous prostatitis Endocarditis—portal of entry unknown	7th	None	140 cc 1 v over 3 days	72 hrs	Perforated interventricular septum, perforations and vegetation aortic valve, infarct spleen
J N	C	F	24 yrs	Postabortal endometritis	15th	None	160 cc 1 v over 4 days	4 days	Infected uterus, endocarditis, infarcts lungs and spleen
S C	W	M	51 yrs	Pneumonia	16th	None	80 cc 1 v	24 hrs	Extensive bronchopneumonia, vegetation mitral valve
A M	W	M	25 yrs	Endocarditis Admitted in stupor Endocarditis	3rd	None	120 cc 1 v	24 hrs	Vegetation mitral valve, abscess lit ventricle, multiple abscesses spleen and kidneys, petechial hemorrhages skin conjunctivae and G I tract
W T	W	M	30 yrs	Chronic prostatitis? Endocarditis	11th	Exploration of perineal area (no pus found)	240 cc 1 v over 4 days	5 days	Mitral valvulitis, multiple abscesses of brain spleen liver pancreas kidneys adrenals prostate petechiae of skin and conjunctivae
D K *	W	F	5 yrs	Multiple skin abscesses Pneumonia r l Pericarditis	11th	Pericardial taps Pericardotomy Resection 6th lit costal cartilage with drain	300 cc 1 v over 8 days	18 days	Not done
B B	C	F	32 yrs	Primary pneumonia r m l and r l l	16th	None	200 cc 1 v over 9 days	10 days	Bronchopneumonia, multiple abscesses of rgt lung
C K *	W	F	3 wks	Abscess of gums Sinusitis (ethmoid and antra)	18th	Incision rgt tibia	10 cc 1 v	24 hrs	Not done
S B	W	F	16 yrs	Pneumonia l u l Chemosis lit eye Abscesses lit faec	5th	None	200 cc 1 v over 4 days	4 days	Thrombosis lit sinus, basilar meningitis etc
J P	W	M	8 yrs	Edema rgt eye Painful swollen rgt shoulder Coma	4th	None	60 cc 1 v over 1 day	36 hrs	Not done

* Skin tests with carbohydrate were made only on these two patients—they were negative

venously, a total of 300 cc being given in all, but without avail Autopsy was not allowed

ANALYSIS OF THE FATAL CASES OF INFECTION

The data dealing with fatal cases will be found in Table II

The remaining patients form a miscellaneous group Thus, patient B B, with primary pneumonia in the right middle and lower lobes, had been on sulfathiazole for one week On the sixteenth day serum was started, and five injections, of 40 cc each, were given over a period of nine days The patient died several hours following the last treatment At postmortem examination, the right lung was found to be riddled with abscesses The infection in C K started as an abscess of the gums followed by pneumonia of the left upper lobe and involvement of the ethmoidal sinuses and maxillary antrum A single injection of serum was given on the eighteenth day and the child died on the following morning No autopsy was allowed Patient S B presented, on admission, abscesses of the left face, chemosis of the left eye, with edema of the right eye which apparently followed the "picking of a pimple" on her chin Sinus thrombosis was suspected but not definitely diagnosed On the fifth through the eighth day 200 cc of serum were administered intravenously, with the patient becoming progressively worse On the ninth day the patient died The main pathologic findings were thrombosis of the left sinus, basilar meningitis, and infection of the petrous portion of the left temporal bone The infection in J P was rapid and fulminating, the whole course covering five days Unfortunately, permission for postmortem examination was not granted, and it, consequently, is not clear exactly what happened The chief complaint was pain over the right shoulder, and the boy was in coma when admitted Blood cultures made obvious the diagnosis of staphylococcal septicemia A single injection of 60 cc of serum was made on the fourth day of illness, and on the following morning the patient died

The evidence offered by the fatalities occurring in this study indicates the unfortunate distribution of patients referred for treatment Thus, only three of the 12 survived more than a week L C and D K who had progressed to a hopeless state because of the cardiac lesions, and B B in whom the pneumonia had not responded to sulfonamides, and was already of 16 days' duration Aside from any other element, that of time alone was a handicap, apparently impossible to overcome

It may be of interest to offer a final analysis of Type-A serum therapy based on the chief clinical manifestation These data have been reassembled in Table III

Endocarditis formed the largest single group with seven patients, all of whom died pneumonia comprised the next largest with five, only two of whom had concurrent septicemia, and four of them recovered, osteomyelitis contributed four patients, three with septicemia and one with transient bacteremia, and all recovered, meningitis with septicemia was encountered twice, and both patients recovered The remaining four patients, all with

TABLE III

SUMMARY OF SERUM TREATED CASES BASED ON CHIEF SYMPTOM

Chief Clinical Manifestation	Number of Patients			
	Treated	With Septicemia	Survived	Died
Endocarditis	7	7	0	7
Pneumonia	5	2*	4	1
Osteomyelitis	4	3	4	0
Meningitis	2	2	2	0
Pericarditis	1	1	0	1
Sinus thrombosis	1	1	0	1
Sinusitis with metastatic pneumonia	1	1	0	1
Undetermined septicemia	1	1	0	1
Totals	22	18	10	12

* Of these, one survived and one died

septicemia, represented a scattering of diagnoses, and all died. The evidence suggests, therefore, that Type-A antiserum offers the most effective assistance toward recovery in pneumonia, osteomyelitis, and possibly in meningitis. In the cardiac complications—endocarditis or pericarditis—the serum appears to be valueless, if survival is taken as a criterion. The remaining cases are too few to allow comment.

Discussion—The foregoing data reveal that 22 patients with severe staphylococcal infection have been treated with specific Type-A antibacterial serum. Bacteriologically, the different infections were associated with a single immunologic type, since all the strains fermented mannite and elaborated Type-A carbohydrate. This suggests that these infections may be treated logically with a univalent serum.

In every patient serum therapy was supplemented by whatever surgical and supportive care was indicated. On this basis ten of the 22 patients survived, and 12 died, indicating a therapeutic effectiveness of roughly 45 per cent or, stated differently, approximately a two-fold increase in the average survival rate usually accepted for such infections. As the figures now stand, it seems that pneumonia, osteomyelitis, and possibly meningitis respond most favorably to the action of Type-A serum.

Analysis of the deaths in this study suggests that the rate of recovery may be an inaccurate expression of the true capacity of the antiserum. The cardiac complications, for example, numbering eight out of 22 (about 37 per cent), or from the point of view of deaths, eight out of 12 (about 66 per cent) indicate, immediately, the particularly abnormal run of patients in this study. Examined in another way, nine of the 12 deaths (75 per cent) occurred within five days following the use of serum. In the light of such a disproportionately large number of patients with hopeless prognosis, it may be that the antiserum possesses a greater therapeutic efficiency than is actually observed in this study.

The skin test with carbohydrate, suggested as an index of sufficient serum therapy, was made in too few patients to be of statistical value. It may be that as far as the results go, however, they confirm its prognostic use. Of

the patients who recovered, the test was positive in five of six, and in the sixth, the last test was made before completion of serum administration. Of the patients who succumbed, the test was negative in three of three cases tested.

SUMMARY AND CONCLUSIONS

(1) Twenty-two patients with severe staphylococcal infection have been treated with Type-A anticarbohydrate serum supplemented with whatever surgical and supportive care seemed advisable.

(2) The strains of staphylococcus isolated in this study fermented mannite and elaborated Type-A carbohydrate.

(3) Of the 22 patients treated as described, ten survived infection and 12 died.

(4) Of the survivals, four were examples of osteomyelitis, four pneumonia, and two meningitis.

(5) Of the deaths, seven were examples of endocarditis, while the remaining were single cases of pneumonia, pericarditis, sinus thrombosis, sinusitis with metastatic pneumonia, and one, not examined at autopsy, of not too clear a diagnosis other than septicemia.

(6) Of the 12 deaths, six occurred within 72 hours, three others within five days, two within ten days, and one within 18 days after first using serum.

(7) While the group treated is small, the indications are that Type-A antiserum has a certain value in the treatment of severe staphylococcal infection, with the best results in this study in osteomyelitis and pneumonia, and the poorest results in cardiac infection.

It is a pleasure to acknowledge the assistance and cooperation received from the Lederle Laboratories, Dr. L. A. Julianelle, of Washington University, St. Louis, and Drs. W. G. Turnbull and J. H. Clark of this hospital.

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ERRATUM

In the ANNALS OF SURGERY 115:47, January 1942 the title of the article by Dr. Herman Charache should read "METASTATIC TUMORS IN THE BREAST." The word "METASTIC" is a typographic error.

BRIEF COMMUNICATION

DISARTICULATION OF THE HIP FOR ENDOTHELIOMA (EWING'S TUMOR) 31-YEAR FOLLOW-UP

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THE FOLLOWING is a report of an Ewing's tumor of the femur operated upon in 1909, and still without recurrence 31 years later. So far as is known, it is the only case of its kind in which so long a period of survival has been recorded. The case is registered with the Bone Sarcoma Registry of the American College of Surgeons, and the original pathologic sections of the tumor have been reviewed by a large number of pathologists, consultants of the Bone Sarcoma Registry, who have agreed as to the diagnosis of Ewing's tumor.

Case Report—Presbyterian Hospital, Vanderbilt Clinic Unit No. 249752, Bone Sarcoma Registry No. 398. H. J., male, Russian Jew, age 22, was admitted, July 22, 1909, complaining of pain in the left thigh of five months' duration. In February, 1909, he first noticed a "squeezing" pain in the medial aspect of the left thigh. It was localized, non-radiating, and not severe. It grew gradually worse, however, with intermittent exacerbations, not provoked by any known activity. Three weeks before admission it had become more severe on walking, and spread from the medial to the anterior aspect of the middle third of the thigh. At times it radiated down the leg to the ankle. It was worse at night. The function of the knee was normal, and flexion and extension of the joint without weight-bearing did not increase the pain.

There were no other symptoms, there had been no injury to the thigh, no operations, and the patient denied venereal disease. His only childhood illness had been measles. He did not use alcohol, tobacco, tea or coffee. There was no history of tuberculosis or malignancy in the family.

Physical examination revealed a well-nourished, muscular young man, with no significant findings other than the local lesion in the middle third of the left thigh. This lesion was a palpable mass, about 6x8 cm, which was bony-hard, immovable, nontender, except to deep pressure, and was apparently attached to the femur. The overlying skin was normal. *Clinical Diagnosis*: Sarcoma of the femur.

Roentgenograms, unfortunately, since destroyed, are said to have shown slight thickening of the periosteum about the center of the shaft of the femur, particularly on its medial aspect. The lesion was regarded as chronic periostitis, associated with osteomyelitis, and operation was not advised. The patient was discharged, July 27, 1909, to report to the Out-Patient Department for observation.

One month later he was readmitted. Since his discharge the pain had increased in intensity and frequency. There was no interference with function other than a sense of insecurity in the thigh, but the pain was so severe that it prevented walking. The mid-left femoral region was now obviously larger than the right.

The findings on physical examination were essentially the same as on the first admission. The reflexes in the lower extremities remained normal. There was no edema. In the midthird of the left femur a hard, smooth mass could be felt. It had not grown appreciably, was not especially tender, and apparently did not involve the overlying muscles or skin. On August 26, 1909, operation was undertaken by Dr. John Hartwell, with a preoperative diagnosis of chronic periostitis of the femur, and a possibility of periosteal sarcoma. The white blood count was 8,750, with 79 per cent polymorphonuclears, and no abnormal white cells.

The tumor was approximately four inches long and occupied the internal, anterior and posterior aspect of the bone. It was fibrous, gristly and attached to the periosteum and underlying bone, from which it was chiseled away *en masse*, leaving a roughened underlying bone surface. It is the reporter's impression that the medullary cavity was not entered. The tumor was soft in places, with plaques of bony-hard substance. It was not obviously vascular and contained no pus.

The postoperative course was uneventful, and the patient was discharged September 17, 1909, 22 days after operation. Coley's serum was administered postoperatively.

Pathologic Report—No 6689. This described the tumor as a bony neoplasm, containing, on the under surface, a milky exudate, apparently softened new growth. Microscopically, it consisted of atypical bone without any haversian systems. It was infiltrated with large cells with large vesicular nuclei and scanty protoplasm, appearing in masses between the spicules of bone. Mitotic figures and multinucleated cells were common.

Pathologic Diagnosis Large round cell sarcoma.

Following discharge the patient was admitted to Memorial Hospital for further treatment with unfiltered Coley's toxin. Beginning with one minim, on November 9, 1909, injections were given in the thigh or buttock almost daily, in increasing doses until on November 30, 1909, the patient received 145 minims. Treatment was then discontinued for six days but was resumed on December 7, 1909, and continued until December 13, 1909. Altogether the patient received a total of 197 minims in addition to the 16 doses previously given at the Presbyterian Hospital. At the Memorial Hospital, from December 14, 1909, until his discharge on December 20, 1909, the patient suffered greatly with pain in his left thigh, headache, and backache, requiring morphine for relief. On December 15, 1909, the white cell count was 14,000, with 86 per cent polymorphonuclear leukocytes.

The patient was readmitted to the Presbyterian Hospital, December 21, 1909, complaining of pain in the thigh, which was constant, and nonradiating, it had grown steadily worse and the thigh had noticeably increased in size. A hard, bony, tender fusiform swelling occupied the midthird of the internal and anterior aspects of the left thigh. The skin and muscles were freely movable over the mass. There was no fluctuation. Over the tumor the thigh measured 47 cm as compared with 43 cm for the opposite thigh. The knee joint was held in a slightly flexed position and could not be straightened voluntarily. The popliteal space was negative and the dorsalis pedis artery was palpable. No palpable lymph nodes were discovered.

Clinical Diagnosis Sarcoma of the left femur.

On December 23, 1909, disarticulation of the left leg through the hip joint was performed by Dr. Joseph Blake. On removing the extensor muscles of the thigh a soft oval tumor, 12x7 cm, was exposed. Its cut-surface was gelatinous and varied in color from pale pink to dark red. It was very friable, and, adjacent to the bone, imparted a gritty sensation. It was firmly adherent to the bone and appeared to spring from the periosteum.

Microscopically (Path No 10087), the tumor was found to be composed of medium-sized round cells, closely packed together and supported by very little stroma. Blood vessels lay in intimate contact with the cells which radiated from the vessel walls in a manner suggesting that they originated from the vessels. Large spaces in the tumor contained necrotic tissue and leukocytes.

Pathologic Diagnosis Round cell sarcoma (perithelioma).

Dr. A. P. Stout has recently reviewed the sections of the tumor and reports as follows: "Sections show that the tumor is composed of long cords of cells, which are usually solid and are separated from one another by strands of fibrous tissue. In a considerable number of instances there is a capillary in the center of a fibrous tissue strand. The fibrous tissue in every instance separates the capillary from the tumor cells. Where the tumor masses are large, the cells, at the greatest distance from the capillaries, are necrotic. The section shows a few spicules of bone. Most of these, in turn, are necrotic, due apparently to pressure from the massed tumor cells which fill the marrow spaces. A few of the spicules suggest new formation of bone. In every instance this is

an irritative and not a neoplastic type of proliferation. The individual tumor cells are, for the most part, rounded, averaging 20 microns in diameter. The nucleus is hyperchromatic, but the nucleoli are, for the most part, small and inconspicuous. Mitoses average one in every high-power field, and in some regions are more frequent than this. The nuclei are centrally placed and are surrounded by thin zones of cytoplasm, which is palely stained and inconspicuous. So far as one can tell from the hematoxylin-eosin stain, there are few or no fibers accompanying the tumor cells except for the broad septa which separates the cords of cells. This picture is characteristic of the bone marrow tumor, variously classified as reticulocytoma, endothelial myeloma, and Ewing's tumor. *Pathologic Diagnosis* Ewing's tumor of the femur."

Subsequent Course—The patient left the hospital February 4 1910, and four months later resumed his work as an engraver. He was then lost sight of until October 2, 1922, when an insurance company, to whom he applied for insurance, requested a report of the hospital findings. The patient has since been followed continuously. Repeated examinations have revealed no evidence of recurrence clinically or roentgenographically. In April, 1937, he began treatments in the Metabolism Clinic for diabetes, which he had recently developed. This has since been controlled under a dietetic regimen.

SUMMARY

A case of Ewing's tumor of the femur is presented, with survival without recurrence 31 years after the patient first presented himself for treatment.

DISCUSSION—DR BRADLEY L. COLEY (New York) said that Doctor Smith's case was unique. There are no other cases on record in the Bone Sarcoma Registry of a proven endothelioma of bone that has survived, as this one has, for a period of over 30 years. Furthermore, there are only 11 such cases in the entire Registry that have survived for five years or more.

As far as treatment is concerned, in the present case both surgery and Coley's toxins were employed. The late Dr. William B. Coley was very much interested in this patient and presented him on several occasions. It was his feeling that the toxins played a definite part in the prevention of distant metastases. In this connection, it might be of interest to mention that of the 11 five-year survivals of endotheliomata of bone listed in the Bone Sarcoma Registry, six received toxins. In this group, of which six were males and five were females, there were no five-year survivals following the use of radiation alone, or toxins alone. In only two instances were surgical measures alone employed. Three were treated by surgery and radiation, one by surgery and toxins, one by radiation and toxins, and four by surgery plus radiation and toxins.

The patient is free of signs and symptoms of local or distant persistence of this tumor on December 1, 1941, thirty-two years after operation.

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EARLY SKIN GRAFTING IN WAR WOUNDS OF THE EXTREMITIES *

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INJURIES OF THE EXTREMITIES OCCURRING in modern warfare often produce wounds with extensive skin losses creating special problems. These skin losses may be due to extensive lacerations by glass or other flying materials due to bomb explosion. Large flaps of skin may be avulsed by bomb blast. Bomb fragments hitting bone create an explosive effect with marked tissue destruction. Deep burns destroying skin have been frequent, due to the great development of mechanized warfare, and the ever increasing use of incendiary bombs.

The characteristic wound seen in air raid casualties is produced by crushing. The patient is crushed by falling building materials causing multiple injuries and compound fractures. Localized thrombosis and gangrene of whole areas of tissue occur—these areas later separate as sloughs.

These wounds may show skin destruction tending to encircle the limb. Following the spontaneous healing of such a wound constriction may result causing circulatory disturbances in the extremity.

The skin destruction may be situated near a joint. Contractures limiting the function of the articulation may be the sequela of such a wound.

In compound fractures, one or many wounds may be found either in direct relation to the fracture site or in the proximity of the fracture. When the wound presents considerable loss of superficial tissue, healing may be incomplete and of poor quality, thus giving an inadequate covering to the fractured bone. Infection may delay healing and consolidation of the fracture. Under plaster such a wound is a natural culture medium, and may discharge an abundant and fetid, purulent exudate of rich and varied bacterial flora. Great delay in the performance of important secondary bone, nerve or tendon surgery may be due to the presence of an unhealed wound under plaster.

When bone is exposed through the loss of superficial covering and perioste-

* Read before the Royal Society of Medicine (Section on Orthopedics)

teum, it becomes devitalized, sequestered, and is open to infection and osteomyelitis. Tendon left uncovered is destined to slough.

To restore normal function to the extremity, in many of these cases, extensive secondary plastic reconstructive operations are often necessary, further delaying the patient's return to active work. It is felt that many of these late complications could be avoided by the early replacement of the skin loss.

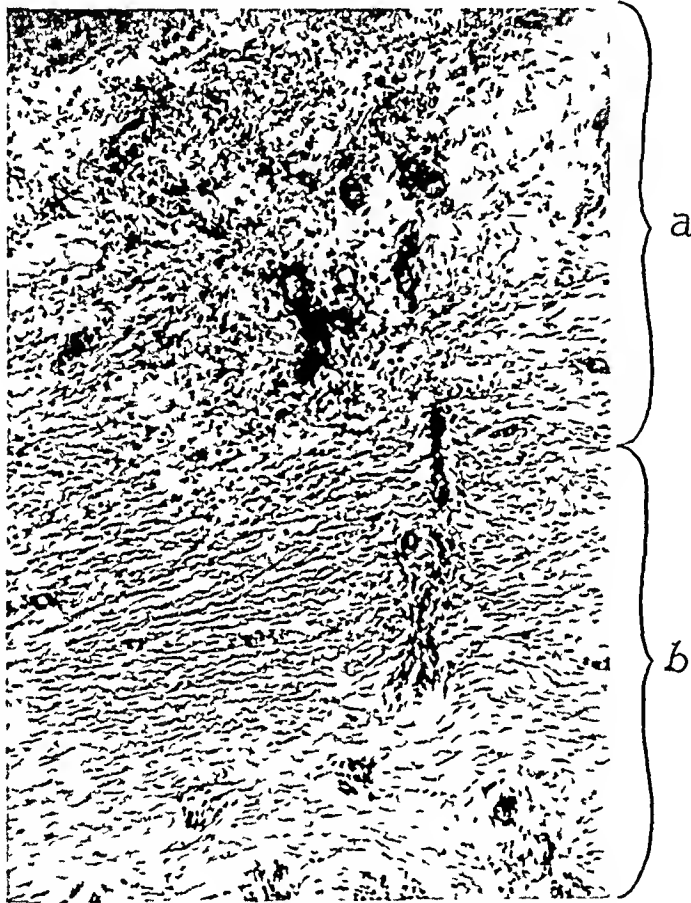


FIG 1—Section of three month old granulation tissue showing development of deep fibrous tissue (a) Chronic inflammatory granulation tissue (b) Deep fibrous tissue layer

Pathology of the Unhealed Wound—The importance of early wound epithelization is brought out by the study of the changes that occur in a wound failing to present rapid spontaneous healing.

In normal wound healing a double regenerative process occurs—that of connective tissue and that of epithelial tissue. Healing is not achieved until the new connective tissue, known clinically as granulation tissue, is covered by a continuous layer of new epithelium. Sections made of young granulation tissue show numerous newly-formed blood vessels and fibroblasts. The latter are situated in a parallel fashion to the blood vessels.

In older granulation tissue, often in wounds, even as early as three to four weeks old, towards the base of the layer of granulation tissue the fibro-

blasts assume a more horizontal direction, thus tending to be perpendicular to the blood vessels. At the same time between the fibroblasts appear connective tissue fibers and collagen (Fig 1)

As the unhealed wound grows older, this deep layer of fibrous tissue tends to increase at the expense of the superficial layer of granulations. Large numbers of capillaries are obliterated, thus depriving the superficial layer of granulation tissue of some of its blood supply. The granulations tend, clinically, to appear cyanotic and edematous due to venous congestion. This first evidence of impaired circulation is improved by pressure over the wound.

The deep fibrous layer slowly invades the superficial granulation tissue, the surface of which tends to become necrotic through defective circulation and secondary infection. Finally, the whole wound tends to become a mass of fibrous tissue.

It can thus be seen that the pathologic picture of an unhealed wound is one of gradually diminishing blood supply, and of progressive increase of fibrous tissue. This produces an increasingly unfavorable base for the spread of epithelium and predisposes the wound to secondary infection.

Rôle of Infection—Infection by pathogenic organisms lead to wound suppuration. The presence of pus appears to be detrimental to epithelial growth, in general. Furthermore, certain organisms seem to have a specific inhibiting action on new epithelium. This is particularly true of various types of streptococci. Colebrook and Francis¹ have reported the remarkable growth of epithelium following the disappearance of the streptococcus from superficial wounds after local applications of sulfanilamide powder.

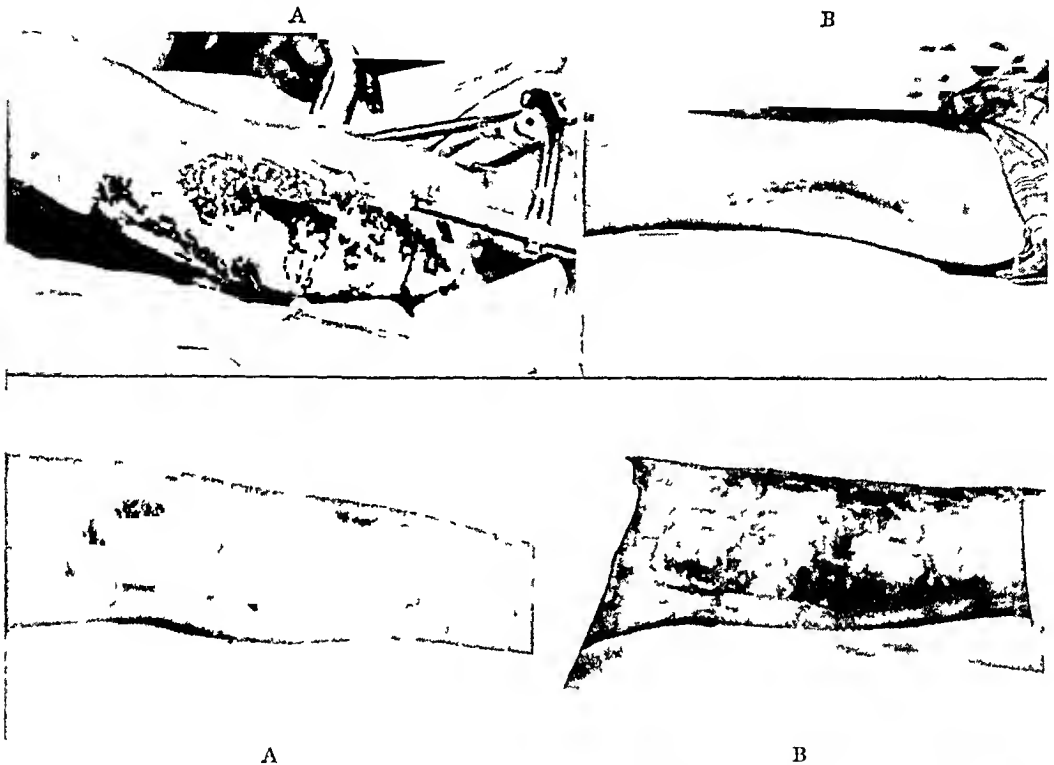
In the stage of acute inflammation, the accompanying edema may prevent the occurrence of contraction, which is a very important phenomenon in wound healing.

Importance of Wound Contraction—Contraction of the wound takes place early in the process of healing, and continues during and after epithelization. Primary contraction occurs following a "silent" or "lag-period" during which, through phagocytosis, the elaboration of enzyme, and exudation of lymph, the wound rids itself of devitalized tissues and foreign bodies. Its occurrence is greatly hastened by the surgical removal of the destroyed tissues by débridement. This contracture is probably due to pull of the elastic fibers within the connective tissue in and around the wound. It is an effort to make the wound smaller, and close it off from the surrounding tissue.

Secondary contraction takes place later in the process of wound healing. When the unhealed wound is invaded by fibrous tissue, connective tissue cells and collagen appear. Contraction proceeds slowly and may continue even after epithelization. The progressive contraction along a scar-line is well known. This late contraction tends to bring the epithelial edges of the wound closer together and is the cause of constrictions, contractures, and deformities of the extremities. The longer the wound remains unepithelized the more marked these deformities will become.

Primary contraction constitutes one of the most important elements of wound healing. It greatly diminishes the size of the wound that is to heal. The defect in deep wounds is filled by surrounding tissue and muscles being "pulled in" as a result of tissue contraction.

Primary wound contraction is such an important element of wound healing that it is possible, to a certain extent, to predict the rapidity and the quality of the wound repair according to whether the wound is situated in a position favorable or unfavorable for wound contraction. Contraction occurs best



Top—FIG 2—(A) Extensive wound of thigh in compound comminuted fracture of femur due to bomb fragment. (B) Example of healing by contraction of wound shown in (A) eight months after injury.

Bottom—FIG 3—(A) Wound of compound fracture of tibia after four months' treatment in closed plaster. Note absence of epithelization. (B) Healing obtained by secondary debridement and skin grafting at time of change of plaster.

when muscle tissue is abundant. Thus, it can be stated that, in a general way, contraction and consequently wound healing are directly proportional to the amount of muscular tissue around the wound. To cite the lower extremity as an example, wounds of the thigh generally heal well, while wounds of the anterior tibial region heal poorly (Figs 2A, 2B, 3A and 3B).

The size of the wound has a bearing on the evolution of healing. Epithelial regeneration through a process of cellular enlargement, multiplication and migration, proceeds at a certain rate. If the loss of tissue is large and if it is in an unfavorable situation for contraction, epithelization of the wound will take a certain length of time during which the fibrous changes, previously described, may occur. It is frequent to see large wounds over the tibia healed but covered by epithelium resting on poorly vascularized fibrous tissue. This poor covering for the bone, which is destined to break down,

appears to bear some of the responsibility for the chronicity of osteomyelitis of the tibia

The "Vicious Circle" of the Unhealed Wound—Where the skin loss is extensive, and when wound contraction is poor, fibrous tissue develops. The circulation of the wound is impaired and infection occurs. Epithelial growth is retarded and more fibrous tissue is deposited. This cycle can repeat itself indefinitely. The result is an unhealed wound.

From these considerations, one is led to conclude that the rapid covering of the wound by epithelium is desirable. If spontaneous epithelial regeneration appears difficult, it is preferable to resort to the artificial provision of epithelium through skin grafting.

INDICATIONS FOR SKIN GRAFTING

A skin grafting operation should be considered

- (1) *When the skin loss is such that it appears probable that impairment of function of the extremity will result*

This applies particularly to wounds about the joint surfaces and to wounds which tend to be circular and are liable to cause contractures and circulatory difficulties.

- (2) *When spontaneous healing of the wound appears improbable*

In the aged and debilitated when the wound is in an unfavorable anatomic situation for healing

- (3) *When rapid healing is desirable*

Skin grafting makes possible at an earlier date secondary operations such as nerve suture or grafting, secondary tendon suture, or secondary bone surgery. In such cases epithelial healing may be achieved in 10 days, when spontaneous epithelization may be prolonged for months. Thus, one is led to feel that skin grafting is justified whenever there is an appreciable skin loss.

SKIN GRAFTING OF OPEN GRANULATING WOUNDS

A study was made of 110 skin grafting operations performed between October, 1940 and June, 1941, at Rooksdown House, and the American Hospital in Britain, Park Prewett Hospital, upon infected granulating wounds. Records were kept of the date and cause of the injury, the date of the skin grafting operation, the bacteriology of the wound before and after operation, and the percentage of success of the skin graft. One hundred per cent represented a complete "take." The operative procedure and postoperative follow-up were noted. Skin grafting was undertaken from two weeks to nine months after injury.

Aside from technical details of fixation of the graft, adequate pressure, etc., two main factors were found to influence the success of the skin grafting.

- (1) Wound infection, and (2) wound fibrosis

- (1) *Wound Infection*—Infection creates suppuration. Purulent exu-

date will lift the graft away from the wound, thus preventing its adherence and "take." Failure, due to suppuration, may be due to the presence of any of the pathogenic organisms. Certain organisms appear to have a specific action upon the "take" of the graft. In the presence of an acute hemolytic streptococcal infection (untreated by specific chemotherapy) skin grafting is generally unsuccessful. Coincident with signs of acute inflammation the wound is filled with serosanguineous pus which displaces the graft from its bed. A dissolution of the layer of fibrin which causes the adherence of the graft appears to take place. This is probably due, as suggested by Colebrook, to a fibrolysin of the streptococcus. A late ulcerative action is observed frequently in grafts that have appeared successful. This is usually found to be due to the hemolytic streptococcus. If uncontrolled it may destroy the whole graft.

The advent of chemotherapy has allowed great control over the hemolytic streptococcus. By the use of local chemotherapy it has become possible to obtain streptococci-free wounds, usually within a few days after initiation of

TABLE I

LOCAL CHEMOTHERAPY AND SKIN GRAFTING OF HEMOLYTIC STREPTOCOCCUS (TYPE A) INFECTED WOUNDS

Total Number of Cases—81

	No. of Cases	Per Cent Skin Graft Take
(1) Failures due to absence of use of local chemotherapy during skin grafting	12	0-25
(2) Failures due to sulfonamides—resistant strain of hemolytic streptococcus	9	0-25
(3) Successful skin grafts in hemolytic streptococcus infected wounds following secondary débridement and local chemotherapy	5	0-70
(4) Successful grafts in wounds previously freed of hemolytic streptococcus by local chemotherapy grafted following secondary débridement and local chemotherapy	55	92
Total	81	

treatment. The wound is freed of purulent exudate by means of dressings, baths, and mechanical irrigation. The bacteriostatic action of sulfanilamide powder applied locally can then take place.¹ After this treatment, it has been possible to perform skin grafting upon wounds presenting cultures free of hemolytic streptococci.

A sulfanilamide-resistant streptococcus persisted in nine patients. Skin grafting performed in the presence of this organism was generally unsuccessful.²

At the time of the skin grafting, sulfanilamide powder was blown over the wound before application of the graft in most cases. The drug was insufflated as a thin layer of powder with Pearce's insufflator. No evidence could be found that the presence of sulfanilamide beneath the graft interfered in any way with the "take" of the graft.

The clinical value of this local chemotherapy at the time of operation is demonstrated by the fact that all complete failures, due to a streptococcal infection, were found to have not had this added protection or to have presented a sulfanilamide-resistant streptococcus, in which the drug had no effect.

EARLY SKIN GRAFTING OF WAR WOUNDS

upon the organism. In five wounds, skin grafting was carried out successfully in the presence of hemolytic streptococci (Type-A), with the aid of local and oral chemotherapy. If, furthermore, one considers that 72 per cent (81 cases) of these granulating wounds were found to have been infected by hemolytic streptococci at some time in their clinical course, the importance of chemotherapy is evident (Table I). Oral sulfanilamide was administered in doses of from three to six grams daily, in the adult, over a period of from three to seven days in those patients whose wounds were recently freed of streptococci (24 cases). The percentage of skin graft "take" was no higher in those cases receiving oral chemotherapy.

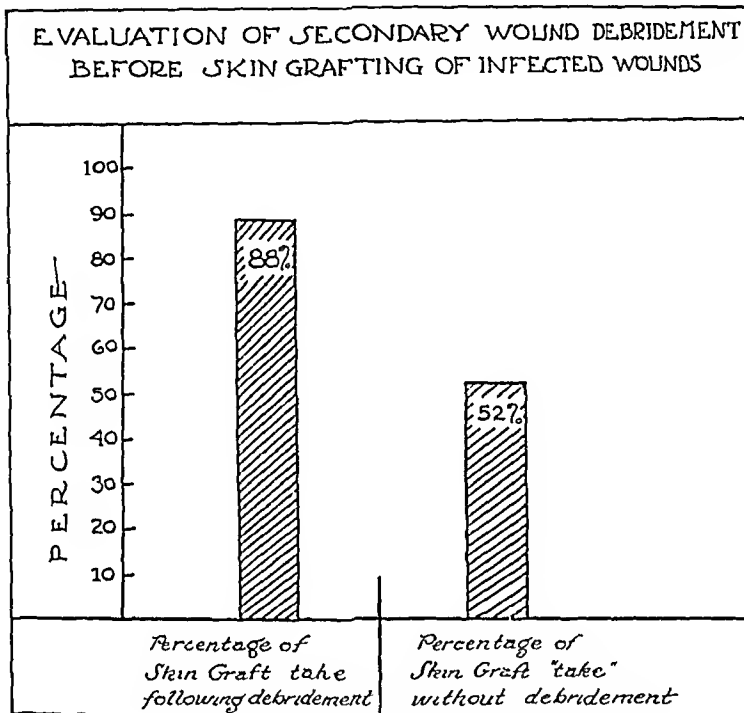


CHART 1

The *Bacillus pyocyaneus* causes failure in most cases where skin grafting is attempted in its presence. Through, probably, a proteolytic action of the organism, the graft becomes very thick, greasy in appearance, and, finally, is removed as a slough. Practical failures were observed in the five cases grafted in the presence of *Bacillus pyocyaneus*. In five other cases grafting was performed after excision of the wound. In two cases, the graft was successful, and there was no reappearance of the organism. In three cases, grafting was nearly completely successful, although a recurrence of the *Bacillus pyocyaneus* was noted. These wounds healed rapidly by second intention. It seems to be a distinct advantage in wounds containing *Bacillus pyocyaneus* to perform excision before skin grafting, as this organism does not appear to thrive in freshly excised tissues. The influence of *Bacillus proteus* upon skin grafting was not observed.

The staphylococcus seems to influence the "take" of the skin graft only in proportion to the amount of exudate produced in the wound. Most cases

of complete "take" of grafts were noted to have presented staphylococci and diphtheroids at the time of operation. However, wound healing and, consequently, successful skin grafting does not depend totally upon the bacterial status of the wound. A wound may be sterile, but may present no evidence of healing.

(2) *Wound Fibrosis*—The production of fibrous tissue in the deep layer of the granulation tissue of the wound diminishes the local blood supply and tends to create a poor base for a skin graft. It would seem preferable, therefore, particularly in older wounds, to excise the wound, whenever this is possible in order to obtain a vascular base for the graft.

Statistics showed (Chart I) that when secondary wound excision was done (54 cases) the percentage of skin graft "take" was 88 per cent. When wound excision was not done (56 cases) the percentage of skin graft "take" was 52 per cent. In some of the cases in this latter group (22 cases) the granulating layer was superficially excised or scraped, thus exposing the fibrous layer before grafting. In these cases the percentage of skin graft "take" was 68 per cent.

SECONDARY DÉBRIDEMENT (WOUND EXCISION)

Secondary débridement of unhealed wounds consists in excision of the whole wound. This includes the infected and fibrotic granulation tissue and the regenerated epithelium until normal appearing tissues are exposed (Fig 4). After this procedure, the wound edges return to the position they occupied before contraction brought them closer together. The graft is applied upon this vascular muscle or fascia. The great objection to this type of procedure in an infected wound is the possibility of a flare-up of a quiescent infection, particularly streptococcal. It is felt that local chemotherapy as an adjunct to secondary débridement prevents such an occurrence. Complete secondary débridement, however, is not always feasible, particularly for anatomic reasons. Extensive wounds over important nerves or vessels, or close to a joint capsule cannot be resected without danger to these structures. If the wound is over bone, there should be no hesitancy in resecting the wound down to periosteum, as skin grafts "take" well on this vascular covering of bone.

TREATMENT WHERE SECONDARY DÉBRIDEMENT (WOUND EXCISION) IS IMPOSSIBLE

Where secondary débridement cannot be done it is necessary to produce, by other means, a wound devoid of suppuration and bring about good local circulation. Attempts are made to accomplish the following:

(1) *Elimination of Suppuration*—Moist dressings, using a wide mesh vaselined gauze or a perforated nonadherent silk, will allow the continuous removal of purulent exudate. The chemotherapeutic effect of the sulfonamides can then take place without being inhibited by the presence of pus. Local chemotherapy is highly successful against the hemolytic streptococcus, and less successful against other infecting organisms such as *Bacillus pyo-*

cyaneus and the staphylococci. A 2 per cent solution of acetic acid has proven the best method of combating the *Bacillus pyocyaneus*. In a number of cases the application of sulfanilamide powder, four times daily, did rid the wound of this organism.

On dressings, it is important to treat the skin around the wound with as much care as the wound itself. Any small crust in the skin around the wound may hide a nest of organisms. Saline baths, either the total-bath around the part, particularly helpful in multiple wounds or the partial limb-bath, at temperatures varying from 98.6° to 110° F prove extremely useful.

The Bunyan envelope applied to the extremity in bed, without the necessity of moving the patient is valuable,³ particularly where other equipment is limited. A 5 per cent hypochlorite solution is used for irrigations. One disadvantage of the Bunyan envelope is the impossibility of applying the proper amount of pressure over the wound.

(2) *Provision of Good Local Circulation*—Firm elastic pressure should be established during the intervals between the dressings or baths, not only over the wound itself, but over the whole of the extremity distal to the wound. The dependent position should be avoided and complete immobilization is essential.



FIG 4—Illustrating secondary wound resection (debridement)

When suppuration is controlled and a good bacterial status is obtained, the superficial layer of the granulations is resected down to the fibrous layer, and skin grafts are applied over a thin layer of sulfanilamide powder. Thus, by eliminating the pus-producing granulations, a greater chance of skin graft "take" is obtained than if the graft were applied to the untouched granulations.

The Choice of Sulfonamide for Local Chemotherapy in Skin Grafting—Sulfanilamide and sulfathiazole were the only two compounds used. Sulfanilamide was preferred for local use in open wounds on account of its higher absorption rate. Sulfathiazole, unless insufflated in very small quantities, tended to "cake." This situation was particularly important under skin grafts. Skin grafts applied over sulfanilamide healed well, over sulfathiazole numerous small areas in the graft appeared to have broken down, possibly due to the unabsorbed sulfathiazole. Sulfathiazole was used, however, where a slow progressive absorption was desired as in a wound under closed plaster. In such cases the drug was found in the blood for as long as three weeks.⁴

Observations on Epithelization—The "Closed Plaster" Versus The

"Open" Treatment of Wounds Under plaster the wounds received complete immobilization and adequate pressure, which controlled systemic infection and favored local circulation.⁵ Local infection was not controlled as evidenced by the purulent exudate containing a rich and varied bacterial flora.

The "closed plaster" appeared to favor, to a high degree, the connective tissue repair of the wound. It was a constant surprise at the change of plaster to see the vascular-appearing granulations under the pus. It did not, however, seem to favor epithelial regeneration, which was very slow. Some wounds, after months in plaster, showed little new epithelium. The epithelium, furthermore, appeared of poor quality, thin, and could easily be wiped away with gauze.

Generally speaking, the wounds that did heal well under plaster appeared to do so by maximal contraction and by minimal epithelization. It is felt that these facts are explained by the fact that the stagnation of purulent exudate is unfavorable to epithelial growth.

Attempts were made to dress the wounds of compound fractures through windows cut in the plaster. This method proved unsatisfactory. Local edema occurred in the wound, it was found difficult to keep the area surrounding the wound clean, and exudate tended to diffuse under the plaster. To expose the wound adequately it was often necessary to cut a window so large as to menace the stability of the fixation.

Wounds presenting skin losses were frequently observed under plaster where, because of their unfavorable anatomic position and the extent of the skin loss, epithelial healing could only take place, if at all, after a long time-interval. During this time the increasing fibrosis would be such as to seriously impair the circulation of the limb by constriction, and to produce wound healing of poor quality which is destined to break down repeatedly. Other cases were observed where unhealed superficial tissue losses under plaster held back the performance of important secondary surgery on the bones, the nerves or the tendons.

It became evident that in such cases great benefit would be derived from successful skin grafting of the wounds.

Secondary Skin Grafting in Compound Fractures—In these cases, the wounds were observed when the plaster was changed and cultures were taken. If grafting of the wound appeared indicated, plans were made for this procedure at the next change of plaster. After removal of the plaster, the wound and surrounding skin were thoroughly washed, and all exudate, dried pus, and crusts were removed. A skin graft was then removed from one of the thighs. A total débridement of the wound was performed, in which all tissue down to healthy muscle, fascia or periosteum was removed. Sulfanilamide powder was then applied with Pearce's insufflator and the skin graft immobilized with a pressure dressing and bandage. A plaster encasement was reapplied to the extremity. On removal of the plaster from four to six weeks later, skin graft "takes," varying from 70 to 100 per cent were found (Fig 5A and B). This type of procedure was carried out in 11

cases presenting extensive wounds in relation with compound fractures (Table II)

TABLE II
SKIN GRAFTING OF INFECTED WOUNDS OF COMPOUND FRACTURES

Case No	Type and Cause of Injury	Primary Treatment	No of Days between Injury and Skin Grafting	Secondary Débridement before Skin Grafting?	Bacteriology at Time of Skin Graft	Percentage of Skin Graft "Takes"
1	Compound fracture of rt tibia and fibula (Motorcycle accident)	Débridement Reduction Sulfanilamide powder in wound Closed plaster	35 days	Yes Wound of anterolateral aspect of leg 8x9 cm	<i>Staphylococcus aureus</i>	90
2	Compound fracture rt ulna and radius (Bomb fragment)	Débridement Reduction No sulfanilamide powder in wound Closed plaster	91 days	Yes Two wounds encircling forearm 5x7 cm each	No growth on cultures	100
3	Compound fracture of tibia (Tank crash)	Primary attempt at closure of defect by plastic using two lateral flaps Closed plaster	37 days	Not done Wound 10x15 cm	Few <i>B pyocyaneus</i>	0
4	Same case as above	Same treatment as above	56 days	Yes Same wound 10x15 cm	Few <i>B pyocyaneus</i>	80
5	Compound fracture upper end rt radius (Bombing)	Débridement Reduction Closed plaster	39 days	Yes Upper lateral aspect of rt forearm 8x13 cm	<i>Staphylococcus aureus</i> and <i>albus</i>	100
6	Compound fracture upper 1/3 of tibia (Motorcycle accident)	Treatment same as above	Treated 8 months in closed plaster Unhealed	Yes Superior anterolateral aspect rt leg 18x9 cm	Few <i>Staph aureus</i> and <i>B pyocyaneus</i>	70
7	Compound fracture tibia, fibula lower 1/3 (Motorcycle accident)	Treatment same as above	32 days	Yes Anterolateral aspect leg 10x12 cm	Hem strep, <i>Staph albus</i>	90
8	Deep burns and fracture tibia and fibula (Pt pinned in bombed house by fallen masonry burned by coals from fire)	Closed plaster without débridement	14 days	Yes Removal plaster Sec débrid two areas 10x12 cm	<i>Staph aureus</i> Diphtheroids	85
9	Fracture dislocation head of radius Open wound lft elbow (Crushing injury sustained in bombed house)	Resection head of radius Débridement Sulfanilamide powder Closed plaster	15 days	Yes Saline soaks for 3 days, then skin grafting after conservative sec débrid removing sloughs Sulf powder Left elbow 26x15 cm	Few hem strep Type-C, and few <i>B pyocyaneus</i>	85
10	Compound fracture rt tibia and fibula lower 1/3 (Motorcycle accident)	Same as above	41 days	Yes Anterolateral aspect of rt leg, small area bone exposed 10x13 cm	Hem strep few <i>Staph aureus</i> and diphtheroids	100 except for area over bare bone
11	Compound fracture of left tibia and fibula (Bombing)	Débridement Reduction Closed plaster	22 days	Yes Ant aspect leg, skin grafting Closed plaster 6x9 cm	Hem strep	70

This method of skin grafting wounds of compound fractures interferes in no way with the routine closed plaster treatment It brings, however,

to this method of treatment, the one element in which it appears deficient, namely, epithelium

Removal of Sloughs, Particularly in Burns—Wounds that have not been primarily debrided often present large sloughs. These sloughs should be treated surgically by secondary debridement followed by immediate skin grafting. This situation is particularly frequent in severe burns where it is difficult to estimate, at the onset, how much tissue damage has taken place. If immobilized in plaster for ten days to two weeks the slough delimits itself and can be debrided and grafted at that time. This secondary debridement obviates the necessity of waiting for these sloughs to separate spontaneously. This may take weeks during which much time is lost, wound fibrosis is developing, and secondary infection may supervene.



FIG 5—(A) Wound of compound fracture of tibia. (B) Appearance of wound after secondary debridement, skin grafting and immobilization in plaster for four weeks. The skin grafting has been done during a change of plaster, thus interfering in no way with the routine closed plaster treatment of the fracture.

Secondary Skin Grafting in Compound Fractures Treated by External Skeletal Pin-Fixation, without Closed Plaster—In such cases the wounds can be treated by local chemotherapy, and other methods, under conditions similar to those found in skin grafting of open granulating wounds as described above.

(1) *Primary Débridement Primary Skin Grafting*—The most opportune time to provide the wound with a skin covering would appear to be at the time of the primary débridement. After resection of all the devitalized tissue and removal of foreign bodies, thus, creating a saucer-shaped wound, a skin graft is laid into the wound and held in position by the firm even pressure produced by cotton-wool or sponge. The plaster can be applied immediately over this dressing or a bandage including not only the wound area but the whole limb can be used for fixation before the application of the plaster.

The compound fracture is then treated by the closed plaster method, the plaster being changed at the desired time-interval. The skin grafting has in no way interfered with the routine closed plaster treatment, but adds to this method the great advantage of an epithelized wound.

(2) *Secondary Débridement Secondary Skin Grafting*—Under the stress

of conditions prevailing at the time the patient is received at the hospital (air raid), in order to save time, it may be preferable to perform the primary débridement, use the local chemotherapy in the form of sulfanilamide powder or a gauze dressing saturated with the drug in the wound, then apply the plaster and postpone the skin grafting until more time is available. It is possible that the tenth day may be the most suitable time for this procedure. The plaster is then removed and a skin graft applied.

Often it is impossible in crushing injuries, or in deep burns, third degree, to distinguish the extent or the depth of the tissue destruction. This is particularly true in burns. In some burns, it is true, the white, dead parchment skin is obviously destroyed, nor can there be any doubt when there is marked charring of the tissue. A primary débridement followed by a primary skin graft constitutes the treatment of choice. If there is doubt, however, as to the extent or the depth of the burn, the extremity can be immobilized in a skin-tight plaster. This gives the injured extremity rest and adequate pressure, and the plaster protects the wound against cross-infection. This plaster immobilization is carried out for ten to 15 days. At this time a slough will have appeared, delimiting the area of devitalized skin and superficial tissue. The plaster is removed, a secondary débridement is carried out, and is followed by an immediate skin grafting procedure.

Contraindications for Skin Grafting—It is evident in many cases where the wound is deep, involving the fascial planes, where suppuration exists, or where there may be a large muscle tissue defect—that it is essential to wait until infection is limited and the connective tissue repair has taken place before skin grafting can be considered.

Types of Skin Graft Used—The most suitable graft is the "thick, razor-graft," also called the "intermediate" or "split-graft." It is cut with the Blair skin graft knife, usually from the lateral or medial aspects of the thigh. This graft is thicker than the Ollier-Thiersch. The latter graft, because of its thinness, has a slightly higher degree of "take." It is, however, less resistant to functional stress than the intermediate graft which gives a strong epithelial covering that in most cases will be permanent.

The "pinch-graft" (Davis) is not suitable in the type of repair considered. It gives epithelization by "second intention," the epithelium spreads out from the individual islands that are grafted. The "pinch-graft" is valuable in extensive burns, if little skin is available for skin grafting, otherwise the best result can be obtained with the "sheet" type of graft, which, if placed under suitable conditions, will take *per primam*.

Removal of the razor-graft requires some practiced skill. Two recent additions to the surgeon's armamentarium have rendered the removal of skin grafts easier, namely, the dermatome (Padgett), and the calibrated razor knife (Humby). The thickness of the graft should be about 14/1000 of an inch, as calibrated by the Padgett dermatome. The graft can be spread over tullegras or vaselined gauze (Gillies) before being applied over the

wound If multiple pieces of graft are needed they are laid on the tullegras slightly overlapping, so as to form a continuous epithelial covering

Covering of Bone and Tendon—Skin grafts are not successful over bone deprived of periosteum Although they will take well on the latter membrane, they are usually unsuccessful over tendon deprived of its sheath In such cases it is necessary to cover exposed structures with a flap of skin consisting of subcutaneous tissue and fat, cut from the side of the extremity and transposed over the defect The wider this flap is made, the better its blood supply

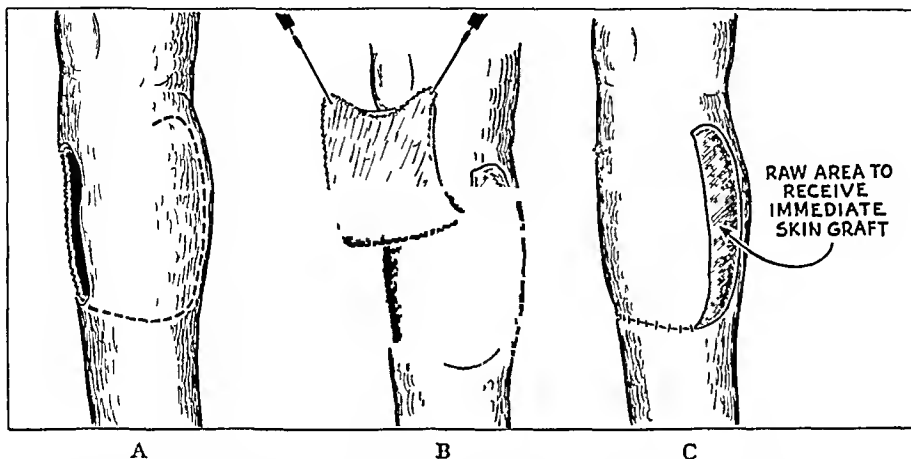


FIG 6—Rotation flap for covering tibial graft (A) Outline of rotation flap (B) Rotation flap is undermined and elevated (C) Rotation of flap is completed and flap covers the tibial defect

In the tibial region the use of local flaps will often allow covering the bare bone A rotation-flap (Fig 6) is suggested as the best type of flap, particularly in long defects Here, the use of parallel advancement-flaps may be dangerous, as they tend to become devitalized because of their length Over the dorsum of the foot, if there is a large defect, local flaps are not available The employment of an immediate direct flap from the opposite thigh is rarely feasible on account of the difficult position of immobilization necessitated in a patient who is often in poor condition In such cases the removal of the outer table of bone will favor the growth of granulation tissue under a closed plaster On these granulations a skin graft may be applied as a temporary dressing Often this skin graft may not stand the strain of walking, or the pressure of the shoe The skin graft can then be excised and a full-thickness flap of skin be applied, taken from the opposite leg

The immediate covering of tendon is imperative to prevent sloughing In small defects of the finger the procedure is employed in which a flap is taken from the side of the finger and used to cover the tendon Then the defect left by the mobilization of this flap is skin-grafted In large defects, where the tendon is uncovered over the whole length of the finger, the digit must be covered by an immediate direct flap, or buried in a skin-pocket in the abdomen or thigh

Avulsed Flaps—Large avulsed flaps, when they present a wide base, may be successfully sutured back into position If the base appears insufficient it

is preferable to remove all the fat, until the base of chorium is exposed, thus converting it into a full-thickness graft over which adequate pressure is applied as for a free graft

SUMMARY AND CONCLUSIONS

War wounds with extensive skin loss are often followed by contractions, constrictions and deformities of the extremities, necessitating secondary reconstructive surgery. In wounds remaining unepithelized longer than from three to five weeks, fibrous tissue changes occur which diminish local blood supply and open the way to secondary infection.

Skin grafting of infected granulating wounds, following secondary débridement and local use of sulfanilamide powder has given success in percentage of skin graft "takes," estimated at 88 per cent in 56 cases. In wounds of compound fractures, skin grafting has been undertaken successfully during the routine change of the closed plaster following secondary débridement and local use of sulfanilamide powder.

War wounds presenting skin losses should be skin-grafted immediately by a primary "skin dressing." This procedure avoids complications and greatly reduces the healing period of the wound.

When immediate skin grafting is not possible or when it is impossible to determine exactly the extent of the tissue destruction, as in deep burns, immobilization in plaster for ten days to two weeks allows the devitalized tissue to delimit itself in a slough, which is then resected and skin-grafted.

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BRAIN ABSCESS OF UNCOMMON ORIGIN—RELATION TO OSTEOMYELITIS OF THE SKULL *

A CLINICOPATHOLOGIC STUDY

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APPROXIMATELY two-thirds of all brain abscesses arise from local infections about the head¹ While most are of otitic origin, about 10 per cent of the total number arise from other foci about the cranium,^{1, 3} notably the frontal sinuses and the soft tissues of the face and scalp To the latter groups, osteomyelitis of the skull bears close relationship, inasmuch as it is often the first complication to arise from the original site of infection It, therefore, appears desirable, in the interest of prophylaxis, to study the mechanism whereby a simple local infection about the head leads to cranial, then graver intracranial involvement

Swimming,^{4 5 6 7 8} and the aspiration of water into the nose, has been the frequent origin of a fulminating infection which led to osteomyelitis, brain abscess, and death, particularly in young individuals, as illustrated in one of our cases Other common conditions that have preceded such involvement are the ordinary cold and its accessory sinusitis,^{9, 10 11} furunculosis of the face and scalp,^{5 12} peritonsillar abscesses,^{13, 13a} and apparently minor head injuries^{2a, 14 15} Simple "office treatments" of the nose and accessory sinuses¹⁶ have likewise been the precursors of intracranial infection, though not as commonly as have radical sinus operations^{16 17, 18}

The importance of uncommon local foci as causes of cerebral abscess has recently been recognized by Carmichael, Kernohan, and Adson,²⁷ who indicated that, aside from isolated case reports, adequate statistics on this group are wanting The relative incidence of cerebral abscesses of various origins among autopsied cases recently reported may be seen from Table I

In a recent review, Mosher⁴ pointed out that fully half of the cases of spreading osteomyelitis of the skull are complicated by intracranial abscesses Of 91 cases of cranial osteomyelitis reported by Lemon,⁹ brain abscess was found as a complication in only 30 per cent In Turner and Reynolds'¹¹ series of intracranial pyogenic diseases there were four brain abscesses, all associated with bony involvement In McKenzie's²¹ series of 48 cases of

* Read at the Combined Meeting of the New York Neurologic Society and Section of Neurology and Psychiatry of the New York Academy of Medicine, May 6, 1941

TABLE I

COMPARATIVE INCIDENCE OF BRAIN ABSCESES OF VARIOUS ORIGINS

Report of	Total No of Cases of Brain Abscess	No Cases of Otitic Origin	No Cases of Rhino-genic Origin	No Cases Due to Other Local Causes	Remarks
Evans ¹	194	109	12	8	Found among 14 543 au- topsied cases
Courville and Rosenvald ²	52	47	7		Found among 15 000 au- topsied cases
Eggston ³⁰	67	37	18	3	Of the last group all followed osteomyelitis of the skull
Bonninghaus	713	631	82		Cases collected from the literature up to 1910
Mayfield and Spurling ¹⁹	52	16	6	7	Based upon a study of 32 patients surgically treated

rhinogenic osteomyelitis of the skull, 45 had followed frontal sinus disease, and brain abscess had developed in ten. The diffuse form of osteomyelitis has been found most frequently in connection with paranasal sinus infections, the more localized forms generally as a complication of local trauma or infection. Microscopic foci of osteomyelitis have been demonstrated about infected nasal sinuses by Kramer and Som³⁶. While diffuse osteomyelitis is uncommon after ear and mastoid disease, minute foci of involvement of the petrous tip have recently been revealed as real or potential causes of brain abscess (Kopetzky and Almour,²² Eagleton,²³ and Fowler²⁴). In our consideration of the pathogenesis of brain abscess, the importance of the intermediate rôle of osteomyelitis in relation to brain abscess will be considered and the therapeutic implications noted.

REPORT OF CASES

Case 1—M. K., male, age 45, was admitted to Beth Israel Hospital, August 16, 1938, complaining of severe sore throat. Examination revealed edema of the pillars and soft palate, and a necrotic grayish patch behind the left posterior pillar.

Neurologic Examination—The patient appeared dull, and presented markedly defective speech and diminution of vision in the right eye. Horizontal nystagmus was present bilaterally. The pupils reacted well and the fundi showed a slight temporal pallor of the disks, but no swelling. There was slight paresis of the lower facial muscles. Ataxia was present in the right finger-to-nose test. All of the deep reflexes were normal and there were no pathologic reflexes.

Course—Excruciating headache developed, which was resistant to all forms of therapy. Hearing became markedly impaired bilaterally, and bone exceeded air conduction, but the ear drums were of normal appearance. The ocular fundi showed some fullness of the veins and some blurring of the nasal side of the disks. While the first four weeks of the illness were marked by an afebrile course, the last week was marked by a sudden and persistent elevation of temperature of 103° to 105° F. The pulse rate was coincidentally elevated. In spite of the administration of large doses of sulfanilamide and repeated spinal taps, the patient died 39 days after admission.

Laboratory Data—R B C 4,500,000, Hb 80 per cent, W B C 9,500, with 75 per cent polymorphonuclear leukocytes, 22 mononuclear cells and five eosinophils. Roentgenologic examinations of the skull were negative.

Spinal fluid, examined September 14, 1938, was clear, under 85 Mm of water pressure, contained 60 mg per cent of protein, 580 mg per cent of chlorides, and 36 mg

per cent of glucose. The cell count revealed eight white blood cells, of which four were polymorphonuclear leukocytes. The smear showed no organisms, and the culture was sterile.

Autopsy—Examination disclosed the presence of a retropharyngeal abscess, with extension of the inflammatory process in the epipharyngeal tissues (Fig 1), osteomyelitis of the clivus (Fig 2). The bony tissue at the base of the skull was partially destroyed. Streaks of thick yellowish-green exudate were noted in the meninges in the region of the cisterna magna and over the right cerebellar hemisphere.

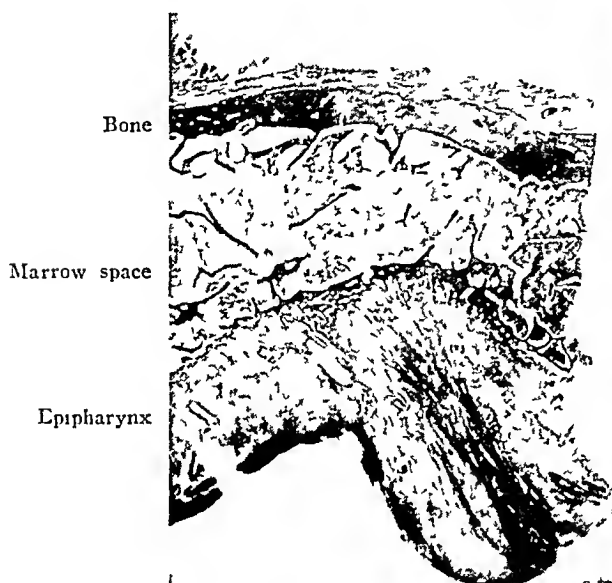


FIG 1—Case 1. Base of the skull showing swollen epipharynx with inflammatory changes. The marrow spaces are between the epipharynx and the bony tissue.



FIG 2—Case 1. Inflammatory process in tissues adjoining the base of the skull. Note the destruction of bone.

Microscopic Examination—Sections of bone removed from the clivus by a Harke incision showed hemorrhage and granulation tissue, with destruction of bone (Fig 2). The connective tissue between the pharynx and bone was widely infiltrated with leukocytes (Fig 2).

The meninges were slightly thickened and were infiltrated by lymphocytes, plasma, endothelial cells and a few macrophages. The vessels of the first layer of the cortex were invaded by the same type of inflammatory cells. The nerve cells appeared normal except for occasional ischemia and slight loss in chromatin. There was slight proliferation of the endothelium of the smaller cortical vessels.

Sections through the centrum ovale disclosed inflammatory foci. The basal meninges and the meninges in the region of the insula and those of the cerebellum and the spinal cord showed the same type of inflammatory reaction as described above. The third ventricle contained inflammatory cells. The ependyma was slightly thickened. Ischemia and other cell changes were noted throughout the thalamus.

Comment—This case illustrates the advance of a peritonsillar abscess to meningitis and abortive abscess formation in the brain. The intermediate relationship of osteomyelitis at the base of the skull was suspected in this instance. A careful search through the Harke incision, on postmortem examination, revealed the presence of a minute focus of osteomyelitis in the clivus (Fig 2*).

* We are indebted to Dr. A. Plaut, pathologist of Beth Israel Hospital, for the studies of the bone specimens in the above case.

BRAIN ABSCESS

Case 2—A W, male, age 28, was admitted to Sydenham Hospital, March 5, 1938. For the previous two weeks he had suffered from sore throat, difficulty in swallowing and some fever. There was a fluctuant mass in the pharynx which was incised and drained of pus. The temperature rose to 106° F, and the patient appeared lethargic.

Neurologic Examination—The patient was aphasic but responded to commands made as gestures. There was neck rigidity and a bilateral Kernig sign. The right cheek puffed out with each respiration. The right corneal reflex was diminished. All of the deep tendon reflexes were absent. There was no Babinski sign. Sensory examination was normal.

FIG 3 A

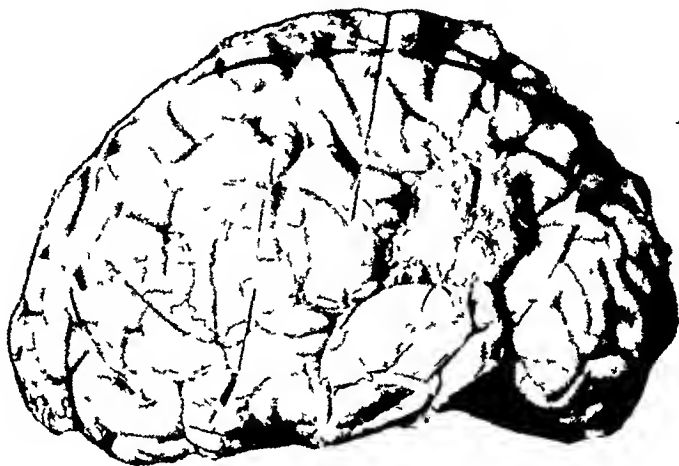


FIG 3 B

FIG 3 A—Case 3. Scar and abscess over the right frontal, pre-motor and motor convolutions.

FIG 3 B—Case 3. Subarachnoid hemorrhage extending from the frontal to the occipital convolutions.

Laboratory Data—R B C 4,590,000, W B C 27,000, with 85 per cent polymorphonuclear leukocytes. Pus obtained from the abscess in the pharynx yielded streptococcus nonhemolyticus on culture. The blood cultures were sterile throughout the illness. The spinal fluid was under increased pressure and contained 300 cells per cu Mm, predominantly polymorphonuclear leukocytes.

Autopsy—Gross examination revealed a parapharyngeal abscess, empyema of the sphenoid sinus, empyema of the left transverse, cavernous, and superior petrosal sinuses of the dura, purulent meningo-encephalitis of the temporal, parietal, and frontal lobes of the brain, multiple brain abscesses of the left cerebral hemisphere and a solitary abscess of the vermis cerebelli. The microscopic examination of the brain abscesses was not different from those described in the other cases.

Comment—Brain abscesses following peritonsillar abscesses are of extremely rare occurrence. Two similar cases have been reported within the past ten years.^{13 13a} The mechanism of spread has been illustrated in Case 1.

Case 3—R. L., female, age 48, was admitted to the Montefiore Hospital, November 24, 1926. An abortion performed 18 years previously had been complicated by pelvic peritonitis, and for 15 years thereafter was followed by multiple abscesses in various regions of the body. A large abscess had formed in the right temple, close to the eye, and had been incised and drained. Operation, in June, 1925, disclosed osteomyelitis of the skull about the outer angle of the orbit. Subsequently she developed headaches, recurrent attacks of vomiting, and pronounced exophthalmos of the right eye.



FIG. 4—Case 3. Abscess destroying frontal and temporal convolutions, invading the basal ganglia (myelin sheath stain).

In May, 1926, she lost consciousness for a few minutes. Examination disclosed weakness of the left hand, ataxia of the left upper extremity with slightly increased deep reflexes on the left. A craniotomy performed at this time revealed an extradural collection of pus and an abscess in the right frontal lobe of the brain. Subsequently flaccid left hemiplegia, hemihypalgesia, hemihypesthesia and hypthermesthesia, a Babinski sign, and convulsive episodes developed. On November 23, 1928 she became confused, apprehensive and incontinent, and died suddenly.

Autopsy—The dura was adherent to the skull at the right temporal region by thin fibrous adhesions, and to the brain over the right frontal, precentral, and central convolutions by dense fibrous tags (Fig. 3 A). The right hemisphere was smaller than the left. On the left side, there was an extensive subarachnoid hemorrhage extending from the precentral convolution to the occipital lobe (Fig. 3 B), involving chiefly the superficial branches of the middle cerebral artery. An abscess measuring 2x2 cm. was present in the right temporal lobe. In some areas this mass showed signs of organization (Fig. 4). The structures adjacent to it (external capsule, internal capsule, caudate nucleus)

were partially invaded, distended, and destroyed (Fig 4) Caudally the thalamus and the lenticular nuclei were compressed and their outlines were indistinct

Microscopic Examination—Myelin sheath preparations showed demyelination of the white fibers of the cortex, internal capsule, and basal ganglia (Fig 4) In the van Gieson and cresyl violet stains, the abscess did not have a well-defined capsule, but disclosed numerous bands of connective tissue traversing it (Fig 5) Between the dense mass of connective tissue and the damaged brain tissue there was a thin inner cellular zone consisting of lymphocytes, plasma, and endothelial cells The brain tissue beyond this area consisted mainly of large collections of inflammatory cells, gutter cells, and congested blood vessels The blood vessels, in the vicinity of the drained abscess and distant from it, showed extensive proliferative changes (Fig 6 A) The perivascular spaces of some vessels



FIG 5—Case 3 The abscess does not have a well defined capsule Notice the bands of connective tissue traversing it (van Gieson stain)

were infiltrated with inflammatory cells (Fig 6 B), in others, all the coats were infiltrated with lymphocytes, plasma, endothelial and compound granular corpuscles (Fig 6 A)

The involved cortical convolutions disclosed a complete distortion in the arrangement of the cyto-architectural layers with marked destructive changes in the nerve and glia cells and proliferation of the vessels The ganglion cells in the cortex adjacent or distal to the abscess had also undergone various pathologic changes from mild chromatolysis, swelling, and ischemia to complete neuronophagia and severe cell changes of Nissl The subarachnoid spaces near and distal from the abscess were distended and filled with red blood cells, lymphocytes, plasma, endothelial and gutter cells

Comment—In this case the brain abscess followed osteomyelitis of the frontal bone in the region of the anterior temporal diploic vein The original focus of scalp infection was probably initiated by pyemia following an abortion, and extending over a period of 15 years

Case 4—J W, male, age 12, was admitted to the Montefiore Hospital, May 1, 1936, with a history of acne and recurrent boils on the neck since January, 1936 A deep abscess had developed in the left side of the scalp, in the preauricular region, and had

been incised by the family physician. In March, 1936, the patient experienced repeated twitchings in the right arm.

Neurologic Examination—This disclosed slight motor weakness, increased reflexes and a Babinski sign on the right side. There were no sensory changes. The disk margins were slightly blurred. The visual fields and acuity were normal.

Course—A low-grade temperature, occipital headaches, and numerous right-sided jacksonian seizures persisted. The papilledema increased. An encephalogram, performed

FIG 6 A



FIG 6 B

FIG 6 A—Case 3. Proliferation of the vessels in the region of the abscess (van Gieson stain).

FIG 6 B—Case 3. Perivascular infiltration as well as infiltration of all the coats of the vessels.

April 2, 1936, revealed distention and displacement downward of the left lateral ventricle. Exploration for brain abscess over the region suspected was negative. Following this, the patient became disoriented and developed sensory and motor aphasia and a right hemihypesthesia. On May 6, 1936, meningeal signs were observed. On reexploration a cerebral abscess was evacuated at the site of the original operation. The patient died the following day.

Laboratory Data—Spinal fluid taken at the onset of patient's illness (March, 1936) was clear, but under pressure of 230 Mm of water. It contained 110 cells, 56 per cent polymorphonuclear leukocytes, 44 per cent mononuclear cells. The total protein was 102 mg per cent, sugar 44 mg per cent, and chlorides 522 mg per cent. A spinal tap taken prior to his final operation was under 310 Mm of water pressure, appeared

turbid and contained 2,000 cells. Culture from the fluid contained the *Staphylococcus aureus* and a gram-positive bacillus.

Autopsy—There was a left temporoparietal decompression with a cerebral hernia and adhesions around it. An extensive subarachnoid hemorrhage mixed with greenish, purulent exudate filled the basal, pontine, interpeduncular and interchiasmatic cisternae. On incising the splenium of the corpus callosum, purulent fluid escaped from the third ventricle. The greatest part of the white matter of the left hemisphere was destroyed and filled by mucopurulent material (Fig 7).

Microscopic Examination—Coronal sections through the striatum disclosed an area of excavation involving the greatest part of the centrum ovale and part of the white and gray matter. The left gyrus cingulus and the first frontal convolution contained



FIG 7—Case 4. Notice the two abscesses and the various zones in the left frontal and cingulus gyri, the marked area of destruction in the white matter and the ventricular infiltration by inflammatory cells.

two separate abscesses (Fig 7). The cavity of the abscesses was surrounded by a dense zone of inflammatory cells, polymorphonuclear leukocytes, lymphocytes, plasma and endothelial cells, and necrotic material (Fig 7). Next to this was a zone less dense consisting of necrotic material and some inflammatory cells (Fig 7). Adjacent to this, there was another dense zone consisting of proliferating vessels, compound granular corpuscles, inflammatory cells, fibroblasts, perivascular infiltrations, and microglia cells (Fig 7). Beyond this zone, there were miliary abscesses, dense areas of inflammatory cells, and occasional proliferating vessels. The adjacent cortical convolutions showed a marked distortion in the arrangement of the cyto-architectural layers and perivascular infiltrations. The nerve and glia cells showed all types of pathologic changes. In some areas there were also numerous *gemastete* glia cells. The meninges were thickened and invaded by the same type of cells as seen in the region of the abscess.

Comment—This case again illustrates the extension of a pathologic process from an infection of the scalp into the bones of the skull and the brain, leading to abscess formation.

Case 5—J. K., male, age 11, was admitted to the Montefiore Hospital, Pittsburgh, Pa., July 4, 1933. While swimming, he had aspirated water into his nostrils. Three days

later he was stricken with malaise, fever, and vomiting, and complained of sharp pain over the right upper eyelid, which was swollen and tender

Roentgenologic examination, July 5, 1933 revealed marked cloudiness of the right antrum, frontal, ethmoidal, and sphenoidal sinuses. The right antrum was punctured and drained of pus which yielded *Staphylococcus aureus*

On the fourth day after admission the entire forehead appeared swollen and red, and both eyelids were pasted shut. The swelling gradually receded, but left, in its wake, two localized fluctuating masses (pericranial abscesses). Incision and drainage of these areas was followed by a chill, nevertheless, clinical improvement ensued, and the temperature dropped to normal levels. During the following week, several more doughy, fluctuating areas, about the size of walnuts, appeared on the scalp in the temporal regions. Roentgenologic examination failed to reveal the presence of bone destruction at this time.

During the third week the patient vomited and complained of dull, diffuse, headache and papilledema was observed. Later, periods of stupor, twitching of the right side of the face, and clonic contractions of the right arm and leg appeared. The left pupil was larger than the right, both reacted sluggishly to light. Hyperreflexia, marked ankle clonus, and sensory impairment were present on the right side for several days. Aphasia was also present.

Laboratory Data—RBC normal. WBC 16,300, with 82 per cent polymorphonuclear leukocytes. Blood cultures were sterile. The spinal puncture yielded a clear fluid, containing 13 cells per cu mm, of which three were polymorphonuclear neutrophils, and ten lymphocytes. Pandy's test was positive for globulin.

Course—During the fifth week of the illness there was a sharp rise in temperature to 104° F, with chills, followed by the localization of another pericranial abscess. A probe passed into a discharging area encountered roughened bone which imparted a feeling like that of rotted wood. Roentgenograms at this time revealed a diffuse destructive process involving both tables and diploe of the frontal and parietal bones (Fig 8). Ocular examination revealed reduction of central vision to 6/12, marked papilledema, enlarged blind spots, and contraction of fields in all meridians.

Despite the extensive suppurative bony involvement and the changes indicative of increased intracranial pressure, the patient continued to improve clinically and was walking about comfortably in the seventh week of his illness. He underwent an extensive sequestrectomy at the Mayo Clinic in October, 1933, and died on that day.

Autopsy—Dr A. W. Adson reported the finding of a diffuse osteomyelitis of the frontal and parietal bones of the skull, and the presence of a beginning abscess in the left temporal lobe of the brain.

Comment—This case illustrates the typical march of events when paranasal infection, contracted after swimming, progressed to cranial osteomyelitis and brain abscess. The diagnosis of bony infection was obvious in the second week of his illness from the occurrence of Pott's puffy tumors of the forehead. At this time the disease was quiescent and the temperature normal. In the light of the present knowledge, it is felt that early and radical surgical therapy of osteomyelitis might have prevented the fatal intracranial complication.

Case 6—H. J., male, age 13, was admitted to the service of Dr S. J. Kopetzky at Beth Israel Hospital, November 24, 1934. A week prior to admission, he had taken ill with a cold, nasal discharge, and temperature of 102° F. Two days before admission, he developed pain above the right eye.

Examination revealed the presence of a thick, purulent discharge in the right nostril and edema about the right eye. On November 26, 1934, the right antrum was punctured. Several days later, the patient developed a chill and severe headache.

Neurologic Examination—One week after admission nuchal rigidity and positive Kernig signs were present. The knee jerks were diminished, but the ankle jerks were active, with a tendency to clonus bilaterally. The abdominal reflexes were present bilaterally. There was no Babinski sign.

Laboratory Data—Roentgenologic examination of the sinuses upon admission revealed evidence of right maxillary sinusitis. RBC and urine showed no abnormality. WBC 15,000, with 74 per cent polymorphonuclears. Two blood cultures taken during the course of the illness showed no growth. The spinal fluid, December 5, 1934, appeared cloudy, was under pressure of 125 Mm, and contained 2,600 cells per cu Mm, predominantly polymorphonuclears.

Autopsy—A thick, turbid exudate was present under the roof and along the inner wall of the right orbit. Microscopic examination revealed the thickening in the orbital

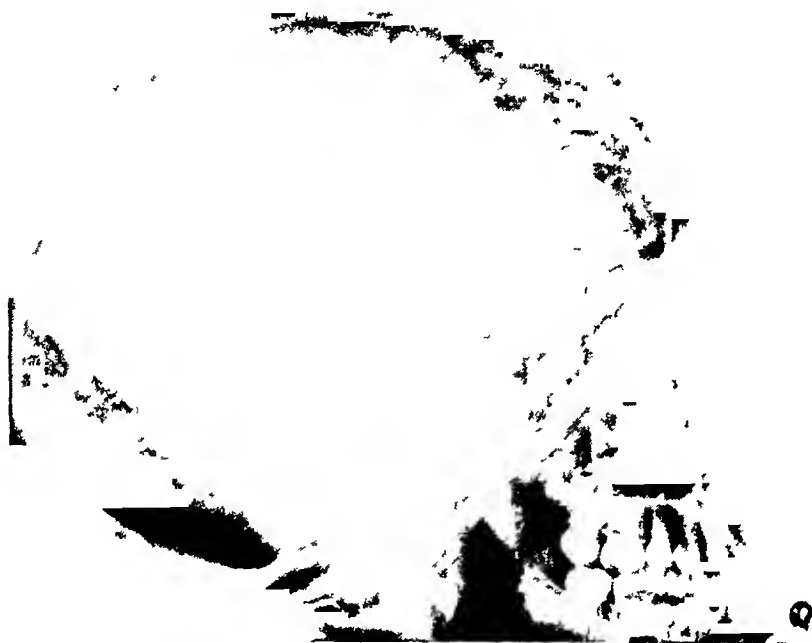


FIG 8—Case 5. Roentgenogram of skull showing destruction of bone as result of osteomyelitis of the frontoparietal region.

roof to consist of old and young osteophytes. The section also showed an area of bone necrosis.

Brain. The dura mater was adherent to the parietal bones. The leptomeninges were tense. The base of the brain, notably in the region of the chiasm, and the cavernous sinus were occupied by a turbid, brownish-green exudate. The left frontal lobe was softened and contained a deep-seated, well-encapsulated abscess 4x2.5x3 cm.

Case 7—S. K., female, age 14, was admitted to the Beth Israel Hospital, February 27, 1935. At the age of three she had undergone a bilateral mastoidectomy and had remained well since. Ten days before admission, a reddened, swollen area had appeared about the old mastoid scar which had been incised by the family physician. Two days later, she developed repeated chills, septic elevations of temperature, and recurring vomiting.

The patient appeared drowsy, complained of diplopia and of burning in the left eye. A positive Kernig sign was present bilaterally. Some weakness was apparent in the left internal rectus muscle. WBC 24,000, with 88 per cent polymorphonuclears. Roentgenologic examination of the skull revealed an area of decalcification in the wall of the left lateral sinus.

The left mastoid region was reexplored, February 28, 1935, and the left lateral

sinus was found exposed because of erosion of the surrounding bone. Postoperatively, the temperature dropped for a few days but the patient became drowsier and complained of pain across the bridge of the nose, radiating down the left cheek. The left pupil was larger than the right, there was drooping of the left upper eyelid, weakness of the left external rectus muscle, and lateral nystagmus. The left corneal reflex was absent. Reoperation, March 8, 1935, disclosed a thrombosis of the lateral sinus. The internal jugular vein was then ligated.

Course—On April 1, 1935, a transitory sensory aphasia suddenly developed and lasted two days. A few days later a series of right jacksonian seizures occurred, lasted four hours, and were accompanied by clouding of consciousness, right hemiplegia, and signs of early papilledema. This episode cleared up within a few days but euphoria and facetiousness appeared. On April 12, 1935, papilledema and hemorrhages of both fundi, and gradual shrinking of the peripheral fields of vision were observed. Right facial weakness of the pseudoperipheral type, anomia, and alexia were present.

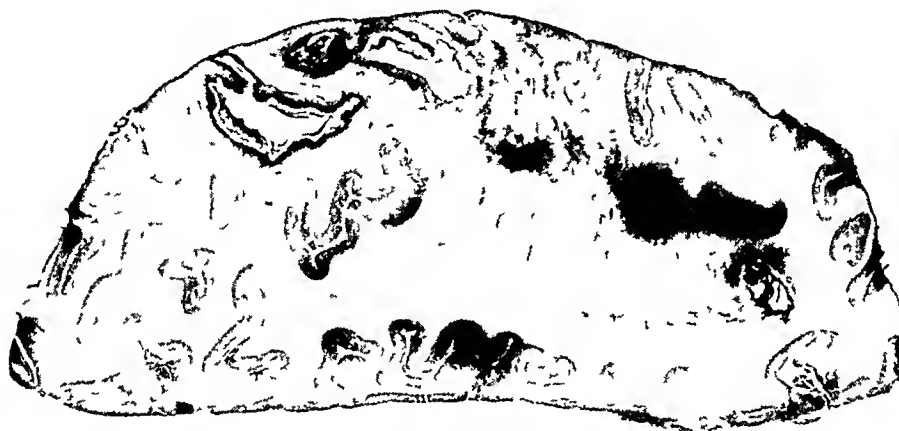


FIG 9—Case 7. Cavitations and brain abscesses in the frontal, motor and parietal regions (cresyl violet stain)

On May 5, 1935, the patient became very drowsy, vomited repeatedly and lapsed into coma. The pulse rate fell to 55 per minute. Surgical reexploration disclosed a large abscess lying very deep in the left temporo-parietal region. The patient died three weeks later.

Laboratory Data—Blood cultures taken on March 2 and 11, 1935, showed no bacterial growth. Spinal fluid, March 7, 1935, was clear, under a pressure of 90 Mm of water, showed a trace of albumin, and 30 cells per cu Mm, of which 22 were polymorphonuclears. No organisms were found on smear or culture.

Autopsy—Examination of the cranial contents revealed the presence of osteomyelitis of the left temporal and petrous bones. The dura mater anterior to the crista galli contained many small grayish-white and yellowish blebs. A similar bleb was situated in the dura mater over the left petrous bone, but showed no perforations. The posterior half of the left lateral sinus contained thrombotic material. The sphenoid sinus was filled with mucopurulent material.

Brain—A large abscess was present in the left temporoparietal region and in part of the basal ganglia. The ependyma of the fourth ventricle was markedly thickened and contained mucopurulent collections.

Microscopic Examination—In a horizontal section through the left hemisphere there were four large cavities (Fig 9), situated in the frontal, motor, and parietal convolutions, involving both gray and white matter. In the cresyl violet preparation, the cavities were lined by an inner pale area surrounded by a more deeply stained zone (Fig

g) The inner pale layer was made up of red blood cells, polymorphonuclear leukocytes, lymphocytes, plasma and endothelial cells. The deeper area consisted of numerous vessels surrounded by inflammatory cells and compound granular corpuscles. The coats of some of the vessels were completely infiltrated by the same type of cells. The meninges throughout the central nervous system were thickened and infiltrated with inflammatory cells.

Comment—This case illustrates the rôle of osteomyelitis of the temporal bone as a precursor of brain abscess. The venous sinuses, explored shortly after the original bone infection, were thrombotic and indicated the venous pathway of intracranial invasion.



FIG. 10—Case 8. Brain abscess of the right orbital convolution and part of the putamen (cresyl violet stain).

Case 8—C. S., male, age 23, was admitted to Beth Israel Hospital, February 27, 1939, with the history of an upper respiratory infection, sore throat, and pain over the right eye and nose since February 10, 1939. Examination disclosed obstruction of the right nasal passage, swollen turbinates, and a mucopurulent discharge from the right side of the nose.

Course—Shortly after admission, the temperature became elevated and nuchal rigidity developed. The left pupil reacted sluggishly to light, the left palpebral fissure was widened, and there was slight weakness of the left facial musculature. Blurring of the left disk and bilateral Babinski signs appeared. The patient became drowsy and suffered from projectile vomiting. The spinal fluid contained 200 cells per cu. mm., 58 per cent polymorphonuclear leukocytes, total protein 67.5 mg., glucose 41 mg. per cent. Ventriculography, performed March 23, 1939, disclosed evidence of a deep fronto-temporal lesion close to the midline. The patient was operated upon, and greenish-yellow pus was removed. Subsequently right hemiplegia developed. The patient became stuporous and expired April 6, 1939.

Autopsy—There was an abscess involving the white and gray matter of the second and third frontal convolutions. Another abscess was found in the right orbital convolutions (Fig. 10). The right ventricle was slightly constricted. The greatest part of the right pallidum and part of the white matter were replaced by an abscess which appeared encapsulated.

Microscopic Examination—Complete coronal sections through the striatum disclosed an abscess involving the putamen and the greatest portion of the white and part

orbital notch and the anterior temporal vein close by. The diploic vessels communicate externally with the venous plexuses of the face and scalp, and internally with the meningeal veins and the adjacent sinus in the dura. The veins in the diploe of the frontal bone are continuous with the veins in the mucous membranes of the frontal sinus, affording ready passage of infection from the paranasal structures to the skull bones. The diploic vessels, especially during youth, are of such caliber as to be easily visualized by roentgenologic examination in 97 per cent of cases (Mosher⁴). Their importance lies in the fact that most of the circulation of the calvaria depends upon the veins and their innumerable small radicals in the diploe, rather than upon the arterial

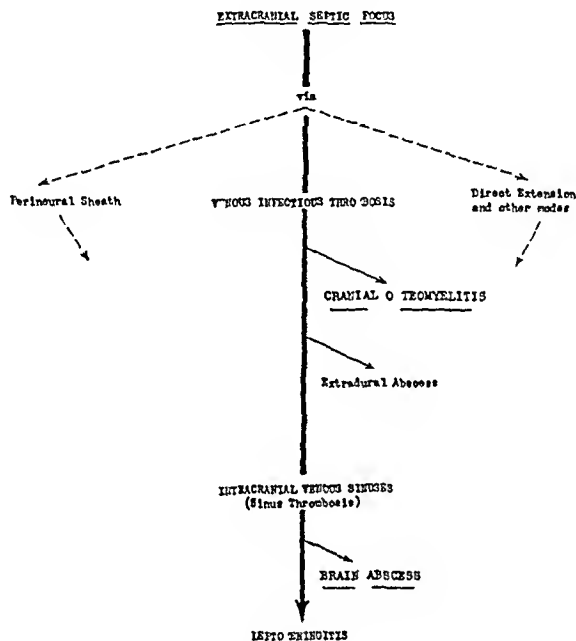


FIG. 13.—Diagram of the direct and indirect pathways leading from local infections about the head to intracranial complications.

supply. Any condition seriously affecting the venous circulation (thrombosis), therefore, jeopardizes the integrity of the bone. This fact is especially well illustrated in Cases 5 and 7 of our series.

The dura mater, which is virtually the inner periosteum of the skull, serves as an excellent barrier to the inward extension of infection. Usually, it is not until the inner table of the skull is involved by a carious process, that the danger of intracranial infection is imminent. In such circumstances the dura is always affected and becomes thickened and granular throughout the entire extent of the lesion in the bones.¹⁶ Further protective adhesions are formed in the arachnoid. Other explanations of intracranial resistance on the basis of the hemato-encephalic barrier (King²⁵), and of immunizing substances in the blood,²⁶ have recently been suggested.

When septic migration takes place from an extracranial source it may take any of several paths (Fig. 13), only one of which will be stressed in this study. Retrograde thrombosis into the emissary veins readily spreads in

the wide-open network of venous vessels and facilitates the rapid extension of the process in all directions. Bone necrosis ensues, generally, first in the outer table, as a result of which there is a discharge of pus under several areas of the scalp (Pott's puffy tumors). The clinical appearance of these fluctuant tumors is illustrated in Case 5. As the inner table is destroyed, similar collections of pus occur between bone and dura (extradural abscesses). The latter process also impairs arterial circulation to the calvarium, and further destruction of bone follows, until the typical worm-eaten appearance of the bone results. The ultimate extent of spread is limited by fibrosis of the marrow space. Mosher⁴ points out that were it not for such zones of fibrosis about the sinuses, osteomyelitis of the skull would more often follow paranasal sinus infection.

The exact sequence between cranial invasion and intracerebral extension is still a matter of some controversy^{27, 29}. It is not yet clear how the infection traverses the meninges and the dural sinuses without gross invasion or destruction of these intervening tissues. Some observers^{2, 11, 33, 34} consider it probable that retrograde infection continues along the venous channels and extends directly into the soft cerebral substance, which is more vulnerable than the tough, highly vascular meninges. In all of our cases, however, some degree of meningeal involvement was found. Osteomyelitis is not invariably followed by cerebral abscess because intracranial invasion is often limited by a zone of reaction within the brain substance (Case 1). Such areas of localized encephalitis constitute, virtually, abortive abscesses, as pointed out by Putnam and Alexander,³⁴ Atkinson,²⁸ and others. When an abscess does develop, it is usually situated in the subcortex, especially in the white matter of the brain, where the veins originate and where cerebral circulation is poorest. The deep location is often a matter of serious surgical concern.

Other pathways of infection have been demonstrated. One is from the nasal cavities along the sheaths of the olfactory nerves²⁹. Another, along the perivascular spaces of the brain, has been suggested by Atkinson,²⁸ Furstenburg,¹⁷ and others, though a true perivascular "stalk" was not found by other observers, notably Carmichael, *et al*²⁷ in a study of 75 cases. Suppuration may extend into the cranial cavity by contiguity or by direct implantation, particularly in the case of penetrating wounds.

The intermediate rôle of osteomyelitis may hold the explanation for the occurrence of a certain number of brain abscesses of obscure origin. Seventeen cases of doubtful or unknown etiology have been recently cited, and four more described by Yaskin, Grant, and Gioff³⁵. The recent studies of Kramer and Som³⁶ on the pathways of infection from the paranasal sinuses have revealed the presence of hidden or microscopic foci of osteomyelitis in the walls of the infected sinuses in ten cases which were complicated by intracranial infection. Minute foci of osteomyelitis in the petrous pyramid have been demonstrated by Fowler,²⁴ and others. Search for very small areas of suppuration in the skull, by special methods of exposure if necessary, as in

one of the cases here described (Case 1) may be helpful in revealing the origin of cryptogenic brain abscesses

Pathologic Considerations—The evolution of a brain abscess may be divided into three phases (1) Phase of localized encephalitis, (2) phase of liquefaction, encapsulation, and (3) extension and rupture. Inflammatory changes begin about the thrombosed vessel in the centrum ovale and progress to necrosis of the tissues and suppuration. Spontaneous resolution and healing with scar formation has been suggested but never proven³⁰. The usual progression is toward walling-off of the infection by a barrier of reactive elements, with the production of a fibrous capsule. Encapsulation begins within a week of infection and generally requires four to six weeks for completion. Surgical experience indicates that the walls of such abscesses are rarely firm enough to give a feeling of resistance to the exploring needle before the second or third week¹⁰. As the pathologic process progresses, the abscess increases in size until ultimately it ruptures into one of the ventricles (as in Cases 4 and 7) or into the subarachnoid space, with resultant pyocephalus or leptomeningitis. An unusual cause of death in the presence of cerebral abscess is that from complicating subarachnoid hemorrhage.

Several factors affect the growth and effective encapsulation of abscesses. Carmichael and his co-workers²⁷ suggest that an abscess must attain a size of 2 cm or more in order to become encapsulated. As a rule, the older the abscess the better the degree of encapsulation. In the most virulent infections, death usually occurs before encapsulation can begin. Abscesses caused by less virulent organisms, particularly aerobes,³¹ last a longer time, and attain considerable size, especially if they are located in one of the silent areas of the brain. Cahill³² has observed that those of the temporal lobe have the thickest lining membranes, while acute cerebellar abscesses are rarely walled off. The largest abscesses in Evans'¹ series were those in the frontal lobe (average 3.5 to 4.5 cm). The effect of medication, particularly sulfanilamide and sulfathiazole, on the acceleration or retardation of capsule formation, although frequently debated, has not yet been demonstrated pathologically or experimentally.

The nine cases of brain abscess presented in this series originated from relatively common infections about the head. One (Case 1) originated from a parapharyngeal abscess, another from a peritonsillar abscess (Case 2). Furunculosis of the face and scalp was primarily responsible for the brain abscesses found in Cases 4 and 7, and secondarily so in Case 3. Four cases were of rhinogenic origin (Cases 5, 6, 9 and 10), complicating in several instances what appeared to be a clinically mild upper respiratory infection. In one of our patients, diffuse osteomyelitis of the skull and brain abscess followed a fulminating sinus infection which developed after the aspiration of water into the nose while swimming (Case 5). Gross or microscopic foci of cranial osteomyelitis were found in those cases where special search for such lesions was made (Cases 1, 3, 5, 6 and 7), while the pathologic process (empyema of a paranasal sinus) strongly suggested the presence of bony involve-

ment in the other cases. Microscopic foci of bone destruction have been demonstrated by others in connection with sinus suppuration^{1, 17, 36}. It appears from our material that cranial osteomyelitis is frequently the intermediate step between a local infection about the head and a complicating abscess of the brain.

Clinical Correlations—Knowledge of the various stages in the pathogenesis of brain abscess may be of great aid in the interpretation of clinical symptoms. As the pathologic processes of the cranial and intracranial extension unfold, certain heralding symptoms appear, and it is from these that the earliest diagnosis of complications might be made. Repeated chills in the presence of an infection about the head, particularly one in the region of the frontal emissary veins, point to possible extension of thrombophlebitis into the skull with the initiation of osteomyelitis. Bone caries are not produced until seven or ten days after invasion, hence, frank roentgenographic changes are not evident within the first two weeks of the illness. The occurrence of pitting edema of the forehead or of localized swellings in the scalp (Pott's puffy tumors) are early and cardinal signs of osteomyelitis in the flat bones of the skull. The spinal fluid during this phase, except for occasional increase in pressure, shows no abnormality.

The phase of osteomyelitis is characterized by a toxic, febrile course, leukocytosis and frequently chills. There is often a latent period of apparent clinical improvement. Then, after days or weeks, septic temperature, headache, and vomiting occur, then nuchal rigidity, focal neurologic signs, increased spinal fluid pressure and pleocytosis indicate the presence of brain abscess. The spinal fluid findings associated with the presence of encapsulated brain abscess in the second to fourth week of the illnesses represented in this series were: Slight increase in the spinal fluid pressure (85 to 230 Mm. of water), cell counts of eight to 200 cells per cu. Mm., with an average of less than 50 per cent polymorphonuclear leukocytes, one plus to two plus albumin, and protein values of 41 to 102 mg. per cent.

According to McKenzie,²¹ Fincher,³⁸ Adson and Hempstead,³⁹ King,⁴⁰ and Bucy and Haverfield,⁷ and others, osteomyelitis of the skull inadequately treated commonly results in fatal brain abscesses. Early diagnosis of osteomyelitis, before the evidence of roentgenographic changes, and complete removal of all infected bone with interruption of the venous channels in the bone which carry the infection inward is the only rational treatment. Discerning surgical management, based upon fuller understanding of the pathogenesis of brain abscess has drastically reduced the mortality from this complication.

CONCLUSIONS

Brain abscess may follow simple infections, other than otitic, about the head. Clinical and autopsy studies of nine cases of brain abscess of uncommon origin are presented. Two cases originated from infections in the pharynx,

three were secondary to furunculosis of the face and scalp, and four were complications of paranasal sinus infection

Osteomyelitis of the skull is frequently the intermediate stage between primary infection and brain abscess. Several illustrative cases are presented.

The pathology of spread is described and correlated with pertinent diagnostic and therapeutic considerations.

Painstaking search for small areas of suppuration in the cranial bones may reveal the explanation for many cases of "cryptogenic" intracranial infections.

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GASTRIC POLYPOSIS

REPORT OF A CASE OF "*polyadenomes en nappe*,"

DIAGNOSED GASTROSCOPICALLY

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GASTRIC POLYPOSIS, by which term single adenomatous polypi are properly excluded, is an uncommon condition. Only about 100 authenticated cases have been reported in recent comprehensive reviews of the literature. Balfour¹ states that in 69,000 celiotomies performed at the Mayo Clinic, of which 8,000 were primarily gastric operations, only one case of gastric polyposis was encountered. Bunn and Pearl,² in a survey of the literature from 1820 to 1925, report 84 cases, five of which they observed personally. The first 49 cases were found only at autopsy. They state that Tsigel³ found 14 benign gastric tumors in 3,000 autopsies. They also quote figures from Doering and from Veise. Doering, in 50 cases involving the entire gastro-intestinal tract, noted that the stomach was involved in only five, while Veise reported 55 cases with the stomach involved in only five, but in none of these was the stomach alone affected.

Cruveilhier,³ in 1833, was the first to give the distinction of a disease entity to gastric polyposis. The first case diagnosed at operation was that of Wegele,⁴ in 1909. Chosiojeff⁵ made one of the earliest clinical diagnoses, in 1912, when gastric lavage revealed blood and particles of polyp. The first roentgenologic diagnosis, according to Balfour,¹ was made by Carmen in 1919. A gastrosopic diagnosis of multiple single polyp was first made by Schindler,⁶ in 1922. We believe this to be the first proven diagnosis of "*polyadenomes en nappe*" made with the flexible gastroscope.

Etiology—Many opinions have been expressed concerning the causative factor of gastric polyposis and certainly the exact etiology is still unsettled. Some observers favor a congenital origin and believe the polyp to arise from fetal anlagen. It is true that in multiple polyposis involving the large bowel there is a definite hereditary factor, but this has not been demonstrated in gastric polyposis. Most authors favor chronic irritation as the inciting cause, and Menetrier⁷ suggests the influence of alcohol. Meyer⁸ reports a case in which syphilitic gastritis may have been the underlying cause.

Pathology—The classic work on the pathology of adenomatous gastric polyp was published in 1888 by Menetrier,⁷ who described two varieties: (1) "*Polyadenomes polypeux*," and (2) "*polyadenomes en nappe*."

"*Polyadenomes polypeux*" are classified as the discrete polyp with independent attachments, either pedunculated or sessile. They are soft, gray, ashy,

GASTRIC POLYPOSIS

brown or red in color, and while their size is variable, it rarely exceeds 2 cm. In number they range from one to more than 300, and, although most common in the region of the pylorus, they may be found in any part of the stomach. Microscopically, they are composed largely of glandular tissue, and the glands are lengthened, often tortuous, occasionally compound, and devoid of pepsin



FIG 1—Photomicrograph illustrating the general pattern as described by Menetrier



FIG 2
FIGS 2 and 3—Roentgenograms showing polypoid type of the gastric lesion

cells. Cyst formation is common when the excretory ducts are obstructed by connective tissue.

In describing Menetrier's second group, "*polyadenomas en nappe*," we can best quote his original paper: "In contrast to some of the smaller pedunculated and sessile tumors arising from simple glandular hyperplasia there is another lesion, essentially a mucosal hypertrophy, in which the glands assume considerable proportions but with the more diffuse and general alteration in-

volving large areas of tissue, forming large hypertrophied plaques rising plume-like above the rest of the mucosa, or even involving nearly the entire stomach, the internal aspect of which then appears tufted and wavy with large folds giving a marked resemblance to cerebral convolutions" He attributes this descriptive phrase to Briquet

Menetrier continues "These are glandular hypertrophies with overgrowth of the epithelial covering, with corresponding increase in the basement membrane and of the interglandular connective tissue. The epithelium is modified into various forms but it is always laid down in regular manner, the glandular

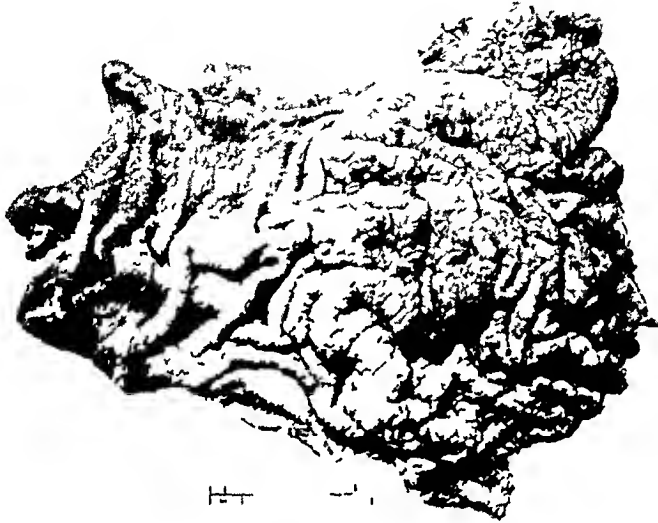


FIG 4—Photograph of the gross specimen

tubes often maintain their upright position, may reduplicate themselves and describe sinuosities, there may be found areas with cystic cavities, but essentially, and it is a cardinal principle, the glandular form persists, the membrana propria is preserved, none of the epithelial cells pass beyond it, and finally, and above all, something which must be considered glandular hyperplasia, never do the proliferated cul-de-sacs pass the basement membrane which is their normal habitat, the muscularis mucosa always forms a limiting membrane for them, easily identified and never broken at a single point

"It is the glandular hypertrophy, and it alone, which determines the thickness of the mucosa. The glands increase in height keeping almost entirely in a straight line, and reach unusual proportions, being five or six times their normal length, while their diameter increases much less and sometimes even diminishes. This long glandular tube is permeable, its orifice is preserved and it is lined with low cuboidal epithelium. The stroma of the mucosa is generally a little thickened and is stretched out like the glands. Rising from the depths are more thickened fibrous bands, each forming an axis around which the tallest glands are grouped in protruding tufts, distinct one from the other and separated by ridges, at the bottom of which are seen the shallowest glands and where the mucus they secrete accumulates

"Such is the general pattern This regular hypertrophy follows the whole extent of the mucosa, thereby becoming too large for the cavity it lines and must, to accommodate itself, fold itself into waves and protruding convolutions which carry in their center prolongations of the cellular tissue It is, therefore, a pathologic and permanent exaggeration of the normal gastric mucosa

"It is a simple hypertrophy, a benign noninfectious lesion Although the lesion is benign, it does have affinities with more malignant states and these lesions may be transformed into epitheliomas and cancers "

Kirklin and Brodeur⁹ aptly state that although polypi generally are benign lesions, they maintain their benign state somewhat precariously Christopher¹⁰ reports an interesting case of this second group which had undergone malignant changes

Symptoms and Signs—All writers on the subject are generally agreed that the symptoms and signs are obscure Frequently, the only complaint is of mild abdominal discomfort, usually developing after meals and in some cases relieved by the ingestion of food or soda Hematemesis and melena may be noted Two characteristic findings, according to Meyer,⁸ are achlorhydria and an increase in gastric mucus which appears much like finely divided, slightly coddled white of egg It has been claimed that these changes are produced by the associated inflammatory reaction rather than by the polypi themselves Frequently, a secondary anemia is present and may be confused with pernicious anemia because of the associated achlorhydria In the collected series of Bienn and Pearl, previously noted, abdominal distress was present in 28 per cent, vomiting, anorexia, constipation, diarrhea and weakness each in about 17 per cent, and hematemesis in 8 per cent

Diagnosis—The presence of achlorhydria, myxorrhoea and gastric hemorrhage demand a consideration of the lesion Essentially, however, the diagnosis must be more conclusively made by the use of the two morphologic aids at our disposal roentgenography and gastroscopy In recent years, increased



FIG 5—Photomicrograph showing the characteristic appearance of a papillary process

roentgenologic diagnosis is evident by the relative frequency with which articles by roentgenologists have appeared in the literature^{9 11, 12, 13, 14 15} This is undoubtedly accounted for by improved roentgenologic technic and more detailed fluoroscopy Nevertheless, in large clinics it is impossible to study minutely every case referred for routine roentgenologic examination of the gastro-intestinal tract, and some lesions will escape diagnosis It is beyond the scope of this paper to describe the roentgenologic signs of gastric polyposis, but we would emphasize the fact that the differentiation of tumors from hypertrophied folds of mucous membrane may present a difficult problem In cases of chronic hypertrophic gastritis, large rugal folds in cross-section may exactly simulate small polypi In one of our cases of diffuse gastric polyposis, or "*polyadenomes polypeni*" roentgenologic diagnosis was not made correctly until after the tumors had been seen through the gastroscope

There can be no doubt that routine examination by gastroscopy of all patients presenting gastric symptoms will make possible earlier diagnoses not only of benign but also of malignant lesions This procedure, in experienced hands, is safe and can be carried out with minimal discomfort to the patient

Differential Diagnosis—Several conditions must be considered in differential diagnosis, among which may be mentioned carcinoma, particularly the polypoid type, lymphosarcoma, hypertrophic gastritis, gastric syphilis, bezoars, and any other lesions which may cause achylia gastrica

Prognosis—As Mencler stated, while gastric polyposis is essentially a benign lesion it does have affinities with more malignant states Brunn and Pearl² in their first paper reporting 84 cases, found an incidence of malignancy of 12 per cent In a later paper, these authors¹⁶ concluded that more than 12 per cent were malignant

Treatment—There is general agreement that surgery offers most in the way of treatment, and partial gastric resection should be performed wherever possible This is particularly true when the incidence of malignancy is considered as something over 12 per cent, in contrast to an operative mortality which should not exceed 7 per cent in qualified hands Brunn and Pearl¹⁶ state that symptoms have been present in certain cases for from 15 to 30 years without any evidence of malignant degeneration However, a sudden increase in severity of symptoms should warn one of the possible onset of this complication

Case Report Hosp No A-03996 The patient, white, female, age 35, single, was first admitted to St Luke's Hospital, November 11, 1938, with a chief complaint of epigastric pain one hour after meals coming in recurrent episodes during the past nine years Nine, six, and five years ago she suffered attacks of pain which did not radiate but were associated with nausea and vomiting Alkalies gave no relief There was no hematemesis nor melena Numerous gastro-intestinal series at various hospitals all showed the presence of a duodenal ulcer On dietary regimens, which she did not conscientiously follow, temporary relief was obtained She had always been subject to nervous attacks, and for the past two months had been nervous all the time, had little appetite, and had lost five pounds, present weight 98 pounds Three weeks ago she had her last attack of burning epigastric pain occurring an hour after meals and associated

with nausea and vomiting for two days. She was placed on a bland diet and given bismuth and soda powders, with prompt relief.

The only other significant facts in the history were that she smoked 20 cigarettes daily, and used alcohol "occasionally." Physical examination contributed little other than that she was a thin, fairly well-developed and well-nourished individual, with slight epigastric tenderness but no palpable mass.

Laboratory Data—Hemoglobin 80 per cent, RBC four million, urinalysis negative, and serology negative. A gastric analysis apparently was omitted.

Gastro-intestinal series, made in the clinic on October 17, 1929 and September 23, 1937, revealed the presence of a duodenal ulcer. A series made October 28, 1938 was reported as follows: "Stomach is large in size and normal in position. In the pars media a polypoid type of growth is seen extending into the lumen of the stomach, beyond the pylorus a regular cap filled. At the sixth hour the stomach had completely emptied. The appearance presented is that of new growth."

Gastroscopic examination was performed November 12, 1938, and our report follows: "The 55° gastroscope was readily passed, and a normal angulus and antrum seen. The pylorus was not visualized. The rugae of the entire posterior wall extending distally to the angulus were finger-like in size, velvety, finely nodular and congested in appearance, actually resembling cerebral convolutions." Never having seen a similar pattern, we were unable to state whether it represented a benign polypoid type of hypertrophic gastritis or a true carcinoma, but we felt that it should be classified as a precancerous lesion.

Operative Pathology—"The stomach was hypertrophied. An indurated, whitish spot on the anterior surface of the duodenum proved to be a chronic ulcer. When the stomach was opened, the mucous membrane of the posterior wall was seen to be hypertrophied and lay in succulent folds. No evidence of carcinoma nor of metastases was seen." After partial gastric resection, a retrocolic Polya-type of gastrojejunostomy was performed.

Pathologic Report—Macroscopic Examination Doctor Knox: "Specimen consists of a stomach measuring 13.5 on the lesser and 18 cm. on the greater curvature. A small portion of duodenum adjacent to the pylorus is included. The serosal surface is clear and pale pink. In the upper portion is an incision into the mucosa measuring 5.5 cm. which has been sutured. A small amount of mesentery is attached. No lymph nodes are found. The mucosal surface of the proximal portion shows hypertrophy of the rugae, giving an appearance similar to the exterior of the cerebrum. The mucosa is intact except at the site of the incision. On section, the mucosa is hypertrophied and there is some thickening of the muscularis.

Microscopic Sections show a portion of the normal mucous membrane of the stomach and also the tall, branching and overhanging rugae, which simulate a papillary adenomatous growth. This area shows an increase in all the cells of the mucous membrane, the epithelium forming long, usually straight, very narrow lumina in most areas. Occasionally the local reduplication is so great as to result in tortuous cysts in the deeper portion of the mucosa. This high degree of differentiation of the cell types of the mucosa distinguishes the lesion from a polyp. The cells are hypertrophied as well as greatly increased in number, but they are regular in outline and normal in staining reactions, and the type of overgrowth does not suggest a true neoplasm. *Pathologic Diagnosis* Papillary, adenomatous hypertrophy of mucosa of pyloric portion of stomach."

The patient has made excellent progress, and when last seen, in December, 1939, one year after operation, she stated that she felt fine, had no gastric symptoms, and had gained 14 pounds in weight.

SUMMARY AND CONCLUSIONS

(1) A discussion of gastric polyposis, and a detailed description of Menetrier's histologic classification are given.

(2) The symptoms and signs of the disease are obscure, but vague.

gastric discomfort, myxorrhoea, achlorhydria and hematemesis may suggest the diagnosis

(3) Roentgenologic and gastroscopic examinations are the chief aids in diagnosis

(4) A case is reported which we believe to be the first diagnosed by gastroscopy, and proved by operation and pathologic examination, to be one of "*polyadenomes en nappe*"

(5) Although the incidence of malignancy is thought to be relatively low, the treatment of the disease should be surgical

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ADENOMA OF THE PANCREAS

CASE REPORTS

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REPORTED CASES of tumors of the islet cells of the pancreas are rather rare. Fiantz¹ was able to collect only 96 cases up to December, 1939. The first case of such a tumor which was recognized and successfully operated upon in the Hartford Hospital was quite characteristic in every detail. We have, therefore, thought it worthy of presentation. A brief summary of three other cases from the records of the Hartford Hospital has been added because of unusual pathologic findings.

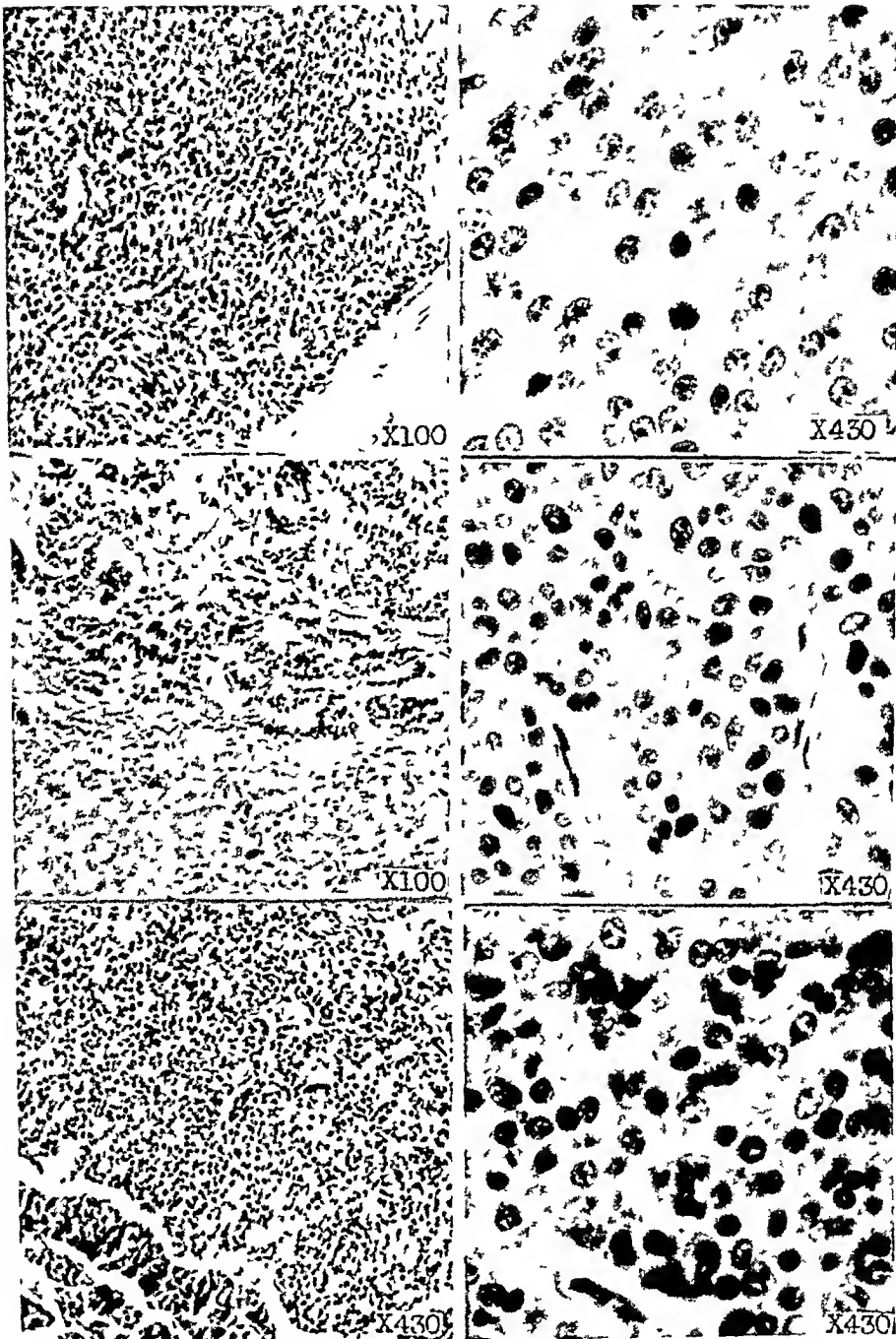
Case 1—Hartford Hospital No 395416. B T R, age 48, American housewife, was admitted, August 15, 1940, with the chief complaint of recurrent attacks of unconsciousness. These attacks occurred usually in the morning and before breakfast, and lasted from one to four hours. They varied in severity from a slight degree of drowsiness and disorientation to semicomatose and even to complete unconsciousness. At times the patient was seen to have difficulty in swallowing or talking. Her speech became guttural or unintelligible. At other times she appeared white, cold, and rigid. Occasionally, she seemed flaccid yet unable to move, and sweated profusely. Her physician found her blood pressure as high as 220/110 during one of these attacks. The patient had been having these attacks with increasing frequency for five months before admission. She was otherwise a well-adjusted, normal person who had had no serious illnesses in the past. On physical examination nothing abnormal was found except a patch of old chorioretinitis in the right eye, blood pressure 148/100, slight enlargement of the heart, and an increase in the deep reflexes.

Complete laboratory examinations of the blood, including blood count, sedimentation rate, and Hinton test, were negative. The analyses of spinal fluid and urine, including urine diastase, were entirely normal. Roentgenograms of the skull, electrocardiogram and electro-encephalogram showed no deviation from normal. The only abnormal laboratory finding was a fasting blood sugar of 30 mg per cent on one occasion and 32 mg per cent on another. The glucose tolerance test showed a fasting level of 56 mg per cent, and the following levels on hourly samples: 148, 182, 182, 136, 56, and 46 mg per cent.

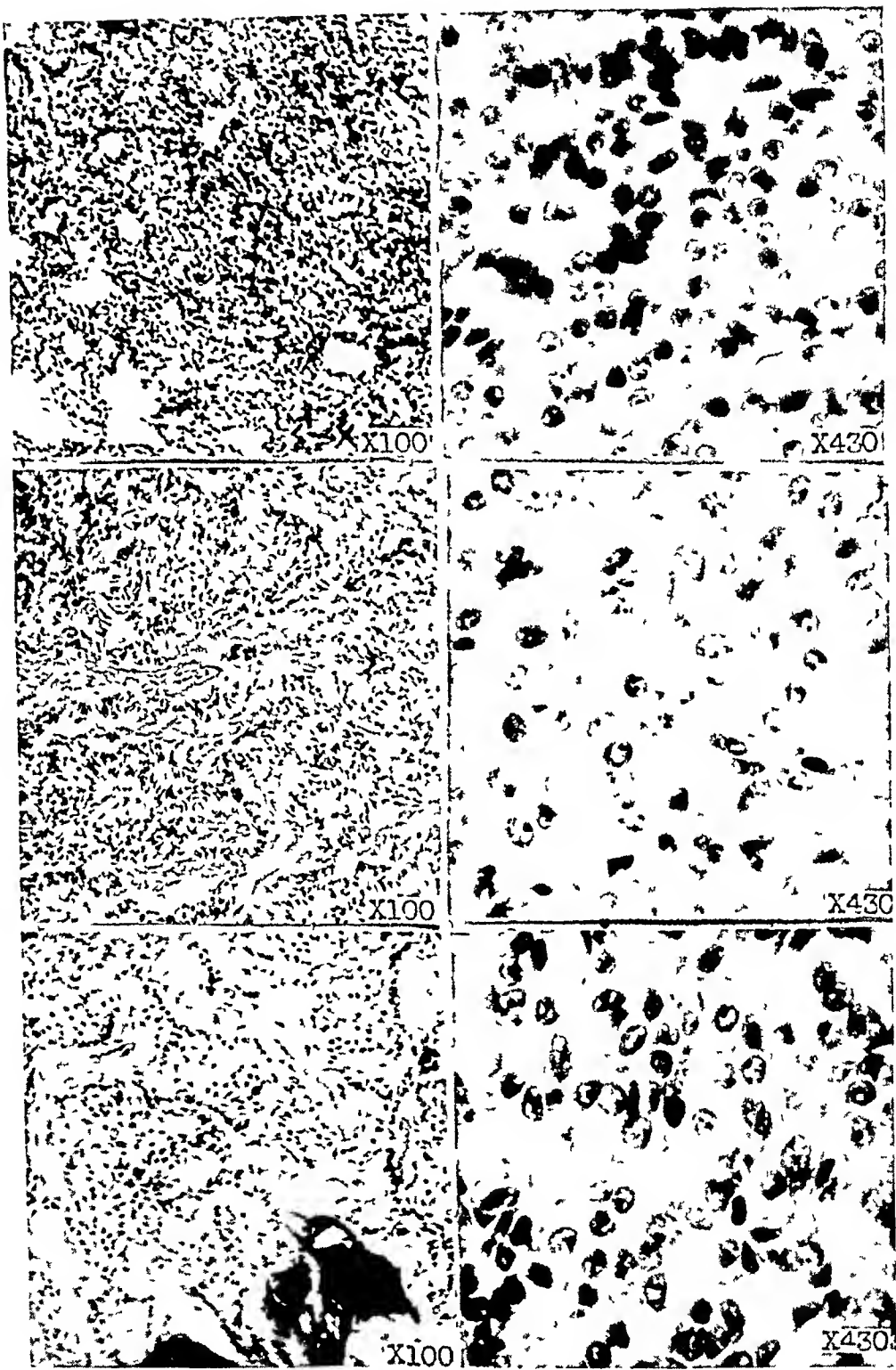
It was found that the patient's attacks could be prevented by the taking of nourishment and that the attacks themselves could be aborted by the intravenous administration of glucose.

Hyperinsulinism due to an adenoma of the islet cells of the pancreas seemed the most likely diagnosis in this case, particularly as it fulfilled the triad of requirements as outlined by Whipple,² namely:

- (1) Attacks consisting of
 - (a) Vasomotor collapse
 - (b) Restlessness, spasm, and convulsions
 - (c) Confusion, disorientation, and coma
- (2) Blood sugar levels of 50 mg per cent, or less, during such attacks
- (3) Relief of symptoms by administration of glucose or taking of nourishment



Top FIG 1—Case 1 Encapsulated islet cell adenoma
Middle FIG 2—Case 2 Metastasis to liver of islet cell carcinoma
Bottom FIG 3—Case 3 Nonencapsulated islet cell adenoma



Top FIG 4—Case 4 Islet tumor cells around vascular spaces
Middle FIG 5—Case 4 Islet adenoma with marked fibrosis
Bottom FIG 6—Case 4 Islet adenoma with calcification

It is generally conceded that surgical removal is the treatment of choice, as prolonged medical treatment has three disadvantages (1) Mental deterioration from recurrent hypoglycemic reactions, (2) personal injury from falls during the attacks, and (3) malignant degeneration. Medical treatment was, therefore, not tried, and the patient was operated upon September 21, 1940.

Operation—Preoperatively, an infusion of 1,500 cc of a solution of 5 per cent glucose and saline was administered. Ether anesthesia was employed, as this mobilizes liver glycogen more effectively than other anesthetic agents. A transverse incision above the umbilicus, through both recti muscles, as described by Whipple was used, and exposure of the pancreas was accomplished by opening the gastrocolic omentum. On the anterior surface of the pancreas, near the inferior edge, and at the junction of the tail and the body was a 1.5 cm, vascular, purplish-red, firm tumor, which was immediately recognized as an adenoma of the pancreas. Careful visualization and palpation of the pancreas revealed no further pathology. By sharp and blunt dissection the tumor was excised, bleeding was controlled with fine silk ligatures, and the abdomen was closed in layers without drainage, using interrupted silk sutures.

Postoperative Course—The patient made an uneventful convalescence, and was discharged two weeks after operation. The postoperative fasting blood sugars ranged between 72 and 95 mg per cent. Chart 1 shows, graphically, the pre- and postoperative fasting blood sugar readings. Follow-up of nine months on this patient revealed complete relief from her attacks.

Pathologic Examination—*Gross* The specimen was a lobulated tumor, 1.5 cm in greatest diameter, partially surrounded with a delicate fibrous capsule. *Microscopically*, sections (Fig 1) showed a cellular tumor with moderate sized oval granular nuclei and prominent nucleoli. The cells were similar in type to the islet cells in the adjacent pancreas. Mitoses were rare. There was a vascular stroma of fibrous tissue separating the lobules, and in most places a well-defined fibrous capsule. There was no evidence of invasion into the pancreas, but in one area there were tumor emboli in vascular spaces.

A review was made of the Hartford Hospital records, and three other cases of tumors of the islands of Langerhans were found.

Case 2—Hartford Hospital No 215803 W H, age 73, white male, was admitted to the medical service, in 1928, because of morning fainting attacks for three weeks previous to admission.

Course—Patient was unconscious on admission and only lived three days. One hour before death his blood sugar was 21.4 mg per cent.

Autopsy—No 452 Revealed a 3 cm carcinoma of the islands of Langerhans in the tail of the pancreas, with metastases to the liver and regional lymph nodes.

Pathologic Examination—*Microscopic* Section showed a tumor composed of masses of cells surrounded by a dense avascular stroma. The cells had small, oval, granular nuclei and were similar to the islet cells in the adjacent pancreas. Mitoses were rare. There was little anaplasia, but definite tumor cell infiltration of surrounding fibrous tissue and pancreas. Some of the larger blood vessels contained groups of tumor cells. In places there was degeneration of amorphous hyaline fibrous tissue, with calcification. The metastases in the liver (Fig 2) and lymph nodes were similar in cytology to the original tumor.

Case 3—Hartford Hospital No 276892 A P, age 59, white male, was admitted to the medical service, in 1933, because of morning dizzy spells, collapse, sweating, disorientation, and convulsive spasms for seven years. These attacks were relieved by the intake of sugar. Fasting blood sugar specimens varied from 26 to 55 mg per cent.

Operation—July 11, 1933 Dr A M Rowley. A very careful search of the whole pancreas was made but no tumor was found. In exploring the pancreas considerable bleeding was encountered which was difficult to control.

Postoperative Course—The patient died a few hours after the operation from shock and hemorrhage

Autopsy—No 1230 This revealed a 12 cm, partially encapsulated tumor deep in the substance of the pancreas, and 7 cm from the tip of the tail

Pathologic Examination—*Microscopic* Sections of this tumor showed masses of tumor cells, arranged around endothelial-lined vascular spaces, with very little fibrous tissue stroma (Fig 3) The cells resembled islet cells of the adjacent pancreas No mitoses were seen The capsule was completely lacking in places, in fact, there was tumor cell penetration as a mass into the pancreas, but no actual infiltration through the normal tissue No blood vessel invasion was seen

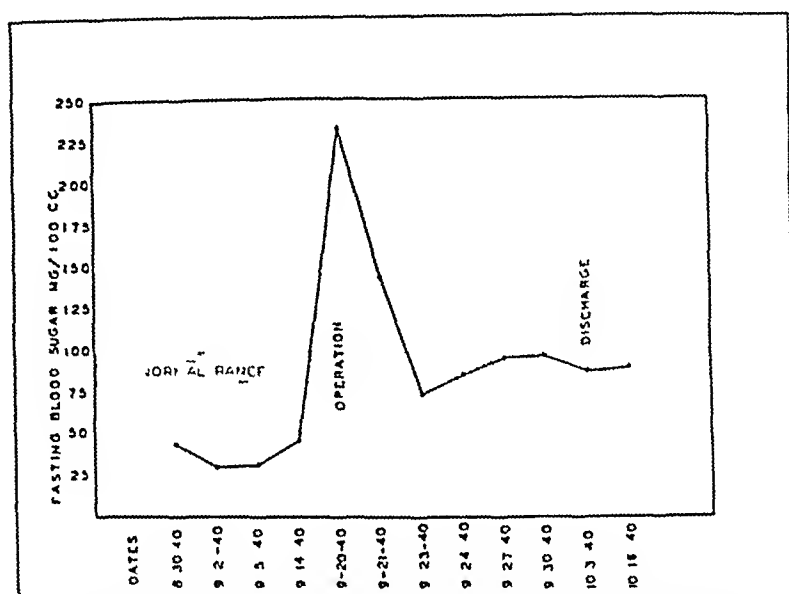


CHART 1—Pre and postoperative fasting blood sugar readings

Case 4—Hartford Hospital No 242564 E E, age 20, white female, was admitted to the Medical Service, in 1930, because of attacks of morning unconsciousness, tremor, and mild convulsions for one and one-half years The attacks were prevented by ingestion of sugar Fasting blood sugar specimens varied from 23 to 57 mg per cent

Operation—December 3, 1930 Dr A M Rowley Three tumors from the pancreas and one from the left adrenal were excised

Postoperative Course—The patient died on the second postoperative day, with hyperpyrexia

Autopsy—No 720 This revealed no significant pathology except the evidence of a recent abdominal operation

Pathologic Examination—*Gross* The surgical specimens showed three discrete tumors of the pancreas, varying in size from 2 to 4 cm The tumor from the left adrenal measured 3 cm in diameter, and was not encapsulated

Microscopically, the three pancreatic tumors showed one well-encapsulated and two partially encapsulated adenomata of the islands of Langerhans There was considerable variation in the cell arrangements in the three tumors, but the cell type was quite similar to, and resembled, islet cells of the pancreas In one, the cells were arranged in ribbon-like cords which surrounded endothelial-lined vascular spaces (Fig 4) In the second, fibrous tissue proliferation separating the tumor cells into small clumps was a more marked feature (Fig 5) In the third, the supporting fibrous tissue showed hyaline change and areas of amorphous calcium deposit (Fig 6) No mitoses were seen In one of the adenomata, tumor cells were found in some of the vascular spaces An acid-alcohol extract of this tumor tissue was injected into rabbits, which initiated an hypoglycemic shock, that was immediately relieved by intravenous administration of glucose

Pathologic Examination—Microscopic Sections of the tumor of the left adrenal showed a primary adrenal carcinoma, the cytology of which differed entirely from the pancreatic adenomata. Extract of this adrenal tumor when injected into rabbits failed to cause hypoglycemic shock.

SUMMARY

A typical case of islet cell adenoma of the pancreas, with relief following excision is reported, and three other interesting cases are mentioned.

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THE MANAGEMENT OF URETERAL CALCULI

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THE MAJORITY of ureteral calculi are formed primarily in the kidney. At this site they may be retained, or may pass down the ureter, where they may become lodged or pass spontaneously into the bladder. Rarely may a calculus develop *ab initio* in the ureter in the presence of diverticula or sacculations, the latter being associated with a stricture in the ureter itself.

That a stone should not develop primarily in the normal ureter appears logical, inasmuch as the crystalloids essential for calculous formation are washed into the bladder by the urinary stream. The origin of a calculus in the ureter, however, may be a calcareous plaque developing on the mucosa, as mentioned by Caulk, in which instance the plaque acts as a nucleus for stone formation. From the standpoint of preoperative and postoperative investigation and care, however, we may consider the kidney itself as the site of calculous formation. To minimize the significance of intensive preoperative study of the etiologic factors involved and their correction and eradication during the operative procedure or during the postoperative regimen, is to invite recurrent formation of stones.

The most acceptable hypotheses of the causation of calculi in the urinary tract are (1) Focal infection, (2) stasis, (3) infection of the urinary tract, especially with urea-splitting organisms, (4) vitamin A deficiency, (5) metabolic diseases, in which an increased excretion of crystalloids occurs in the urine, (6) hyperparathyroidism, and (7) local disease of the renal papillae.

From clinical and experimental observations, it is apparent that no single etiologic factor is responsible for the formation of all calculi. With our present conception of calculous disease, it is essential to ascertain the presence or absence of the factor or factors responsible for stone formation in each case. A presumption of their absence is fraught with the possibility of a high morbidity. Roentgenologic investigations reveal that the majority of ureteral calculi become lodged in the pelvic portion of the ureter. This hesitation in the descent of the calculus may be temporary, in which case it passes into the bladder or becomes impacted, thus preventing further movement. The arresting of the downward progress of a calculus in the ureter may be satisfactorily explained by the anatomic characteristics of the normal ureter. It has been demonstrated in cadavers that the caliber of the ureter varies in its different portions.

Constriction may occur in five locations in the normal ureter (Fig 1), namely, (1) at or just below the junction of the ureter and the renal pelvis, (2) at the point where the ureter crosses the iliac vessels, (3) at the base of the broad ligaments in the female, and the vas deferens in the male, (4) at the point where the ureter enters the external muscular layer of the bladder, the so-called juxtavesical constriction, and (5) at the ureteral orifices. Between

these constrictions the ureter is widened into spindles, the diameter of which decreases progressively downward

In addition to the points of constriction mentioned, physiologic angulations of the ureter may occur at two points. First, at the site where the ureter crosses the iliac vessels and dips downward into the true pelvis, and second, at the *pars juxtavesicalis* which presents a physiologic angulation of from 90° to 135° . Undoubtedly, these conditions in the normal ureter explain, in a large proportion of cases, the incidence of ureteral calculi at various levels in the ureter.

In this series of 350 cases, 77.4 per cent of the stones were observed in the lower ureter, of which 63.3 per cent were in the pelvic portion, and 14.1 per cent in the intramural portion. The positions of the calculi in this total series are shown in Table I.

TABLE I
POSITIONS OF CALCULI IN 350 CASES

Right upper ureter	14 cases
Left upper ureter	16 cases
Right midureter	21 cases
Left midureter	22 cases
Right lower ureter	128 cases
Left lower ureter	143 cases
Bilateral ureteral calculi were present in six cases	
Right lower ureter and left lower ureter	3 cases
Right lower ureter and left upper ureter	1 case
Right midureter and left midureter	1 case
Right midureter and left lower ureter	1 case

MANAGEMENT

The procedures to be utilized in the management of ureteral calculi are (1) Expectant and medical, (2) manipulative procedures, and (3) surgical intervention. Several factors influence the type of treatment to be advocated in the individual case.

Expectant Treatment—In eliciting the history from patients with calculous disease, we are warranted in assuming that a large percentage of ureteral calculi are expelled spontaneously. Many patients cite repeated episodes of pain followed by the passage of a calculus. In the present series of 350 cases, 18.9 per cent of the calculi passed spontaneously during expectant treatment. During this period fluids should be forced and urinary antiseptics prescribed, if necessary. The prescribing of drugs as an aid in the expulsion of calculi in the ureter is recommended by some authors. Hager¹ recommended the subcutaneous injection of 1 cc of 1:2000 solution of prostigmin at three- or four-hour intervals for four doses to stimulate passage of ureteral calculi.

O'Connor² reported the results of treatment with this drug in 52 patients. The cases were selected carefully before its administration. In 30 cases in which expulsion occurred, the procedure appeared to hasten the passage of the stone in 23 instances. Of six cases in which calculi of larger size did not continue to descend over longer periods of time, in five the stone passed into the bladder, and in one it was arrested in the ureteral orifice following the

administration of this drug. In 16 patients, meatotomy, dilatation and multiple catheters or bougies were employed without effecting passage of the stone. In the presence of a large lower ureter, and in the absence of complications necessitating surgical intervention, prostigmin was employed, followed by rapid descent or expulsion of the calculus in 12 of the 16 patients. He concluded, therefore, that of the 66 patients treated, prostigmin was employed as an additional aid in 52, and in 18 of these the clinical response was so striking that the efficacy of the drug in selected cases is beyond doubt.

Scholl,³ in treating 15 personal cases in a similar manner observed, in seven instances that the drug exerted a beneficial action.

Of 19 cases in which I have employed the drug, in eight instances within four days after the medication was prescribed, the stone was expelled from the ureter. In four additional cases the stone passed within one week, while in seven instances the progress of the calculus was not affected.

It is known that in patients who have passed stones previously progressively larger stones may be expelled than would occur when the initial stone passes into the ureter. Similarly, a small calculus that has just occupied the ureter is more apt to pass spontaneously than if it has been lodged in the ureter for a longer period of time.

In patients in whom expectant treatment is advocated, careful observation is essential. Progress roentgenograms to follow the course of the calculus are required. When the patient's symptoms subside, either a complete block has occurred, or urine is passing around the stone into the bladder. If intravenous urographic study reveals a complete block, in which instance the pelvis and calices are not visualized, unless prompt additional treatment is employed, complete destruction of the kidney may result. To delay instrumentation for too long a period of time in selected cases of ureteral calculi, or failure to recommend surgical intervention if deemed advisable, may be attended by little success. Such postponement may be followed by loss of the kidney, or even death of the patient.

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Several factors determine whether manipulative procedures are advisable or surgical intervention is required. These are:

(1) *Economic Status of the Patient*—Just as the economic status of a patient may influence the treatment to be instituted in medical problems ex-

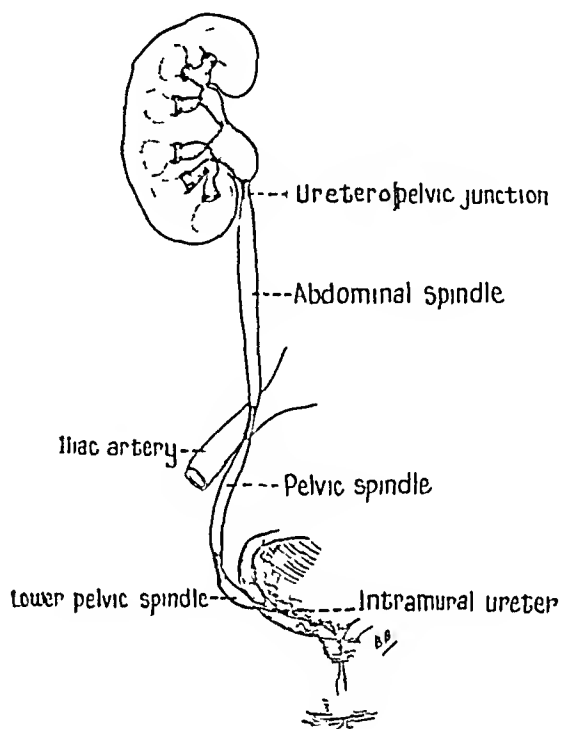


FIG. 1.—Diagram illustrating the sites of constriction in the normal ureter.

traneous to the urinary tract, so may it influence the treatment to be advocated for a patient having a stone in the ureter. A laborer having a calculus lodged in the upper ureter and progressing downward very slowly, or having periods in which the calculus remains stationary, who has repeated attacks of colic necessitating confinement to the home, frequently may be restored to his gainful occupation by surgical intervention at an earlier period than if expectant treatment is advised until the stone is in the lower third of the ureter. In like

manner, individuals whose occupations require considerable expenditure of energy which provokes an attack of colic, because of their possibility of losing employment due to the frequent disability and financial status, may require more immediate relief.

(2) *Size of the Calculus*—As a general rule the larger the calculus the less likely it is to pass spontaneously, and the more frequent will manipulative efforts fail. Obviously, the size of the ureter is of considerable importance with relation to the size of the calculus in determining the progress of the stone.

In Joly's⁴ experience, patients passing stones at varying intervals of time are able to expel progressively larger stones from the ureter. Hinman⁵ states that, generally speaking, stones of more than 1 cm in size in the upper ureter, or more than 2 cm in size in the lower ureter, require operation if they have not been affected by one or two manipulations, or if they have not moved for some time.

In this series it was noted that calculi larger than 1 cm in diameter infrequently pass down the ureter spontaneously. In the absence of back pressure they may be

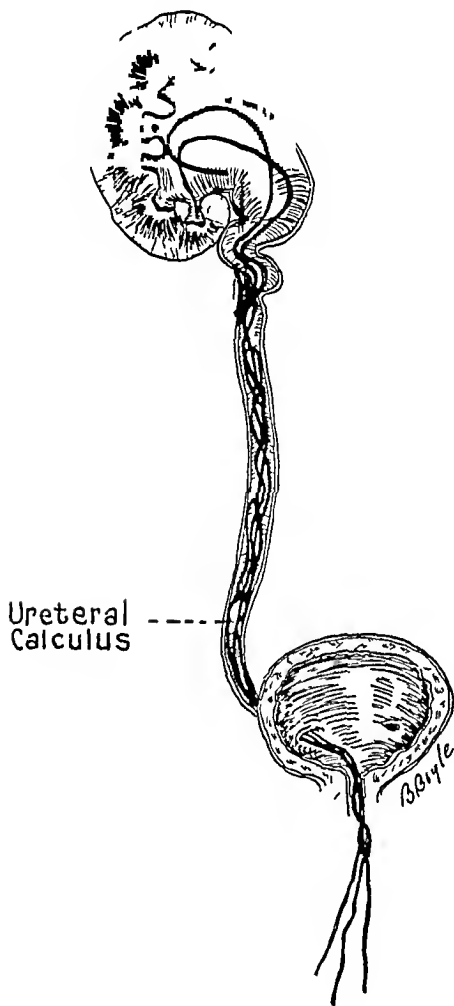


FIG. 2—Multiple catheters utilized in removing a stone from the lower ureter

observed and followed by roentgenographic studies.

The majority of ureteral calculi are small, however, and unless impaction is present or they are attached to the mucosa of the ureter by spicules, they will descend to the lower third of the ureter where, in the absence of complications or contraindications, manipulative efforts may be attempted.

(3) *Position of the Calculus in the Ureter*—A stone in the lower third of the ureter usually is more amenable to manipulative efforts than a calculus in the upper ureter. Where a small calculus is present in the upper or middle third of the ureter, in the absence of complications, it is preferable to permit

the stone to descend to the lower third of the ureter before attempting manipulative procedures

If the stone is over 1 cm in size and has been in the upper ureter, for some time, and remains impacted or moves very slowly, operation is advisable. This is especially true in the presence of infection or increase in hydronephrosis. In some instances only a mild degree of obstruction is present as the urine passes by the irregularities in the calculus, thus producing slight dilatation of the ureter above the stone. This dilatation, however, may be sufficient to dislodge the calculus which then passes into the pelvic ureter. In many instances a stone at this site is treated expectantly or by various manipulative efforts when surgical intervention should have been employed without hesitancy. The mortality is extremely low and the kidney is saved from the ravages of back pressure and infection.

In contrast to stones in the upper ureter, when they occupy a position in the lower third of the ureter, expectancy and manipulative efforts in the absence of contraindications are to be favored. Careful observation is essential, however, as they may remain here for some time, producing but few symptoms or only varying degrees of colic. However, surgical intervention should not be delayed following disappointment in the expectant or manipulative treatment.

(4) *Status of the Kidney Above the Stone*—Continuous evidence of renal changes from back pressure or infection, as evidenced by pain over the kidney, or a progressively enlarging hydronephrosis, as revealed by an intravenous urogram, contraindicates continued conservative manipulative efforts. In like manner, if the urogram reveals that the calculus is producing complete blockage of the ureter, even in the absence of pain, the obstruction must be relieved. If a catheter cannot be passed beyond the stone, surgical intervention is advisable. In cases in which the pelvis of the kidney and calices are not visualized by intravenous urography, it does not imply that a normal or fairly normal function will not be revealed when the obstruction is removed. Joly states that the presence of a coexisting chronic parenchymatous nephritis contraindicates conservative medical management, this condition preventing the forcing of fluids.

(5) *Age of the Patient*—In elderly, debilitated, senile patients, repeated manipulative efforts frequently are not well tolerated and may be attended by severe general reactions. In the presence of an enlarged prostate, cystoscopic manipulation is more difficult and is attended by considerable trauma. This condition may favor an open operation, although the calculus is of a size that manipulative treatment would be employed in a younger individual. In small children, manipulative efforts in selected cases may be employed. Newer instruments have been introduced in recent years to facilitate carrying out such procedures without trauma or difficulty. Again, however, recourse to surgical intervention should not be neglected in selected cases such as congenital anomalies which may render conservative procedures extremely difficult.

The presence of lesions in the opposite kidney, such as obstruction from various etiologic agents, stones, etc., may influence the treatment to be recommended.

(6) *Coeexisting Pathologic Conditions*—Various other factors may influence recommending surgical intervention. The presence of a large cystocele, stricture of the urethra, fibroid uteri, and pelvic tumors, may contraindicate manipulative efforts. In the presence of anuria, the presence of a solitary kidney or bilateral ureteral calculi must be considered. Here we are confronted with an emergency and, if possible, the passage of a catheter beyond the obstruction is of paramount importance in facilitating urinary drainage, the immediate attack upon the calculus being delayed until the crisis is passed.

Manipulative Procedures—In recent years urologic surgeons have been more enthusiastic regarding the manipulative management of ureteral calculi. There are several objectives to instrumentation, and the instrument to be employed is influenced by the purpose of the procedure.

(1) Drainage by passing a catheter beyond the stone to relieve back pressure and to assist in eradicating infection.

(2) Dilatation of the ureter.

(a) Passing a ureteral catheter or catheters beyond the stone and leaving them *in situ* for from 24 hours to three or five days (Fig. 2).

(b) Employing bulb catheters of varying sizes.

(c) Using mechanical dilators, such as the Dourmashkin bag, to dilate the ureter or the orifice below the stone.

(3) Using especially designed instruments for extraction of the stone or extractors, such as the Council, Welland, Howard, or Johnson.

(4) Meatotomy by fulguration or the use of especially designed ureteral scissors.

The large number of instruments available today for the manipulation of stones in the ureter attest to the fact that no single instrument or method is suitable in all instances.

Undoubtedly, experience with the various procedures influences the advisability and the selection of the instrument to be used in a given case.

As has been frequently stated, the manipulation of stones in the ureter is not an office procedure and hospitalization is to be recommended in all cases.

Many types of manipulative procedures are advocated by various authors. I still prefer the use of multiple catheters, and then the Council extractor if the stone is not delivered by means of catheters. The spiral dislodger is especially efficacious in the removal of calculi impacted in the ureteral meatus (Fig. 3). Larger stones lodged in the intramural portion of the ureter may be removed by employing fulguration or especially devised ureteral scissors (Fig. 4). Care and gentleness during manipulation, in order to minimize trauma of the ureter, are important.

After the cystoscopic removal of a ureteral calculus, a ureteral catheter is passed to the kidney pelvis to remain for a period of from 24 to 48 hours. This minimizes the incidence of pain following manipulative procedures.

In a series of 199 cases of ureteral calculi, reviewed a few years ago, it was noted that in 15 cases, or 7.9 per cent, the stone passed spontaneously, in 69, or 34.7 per cent, the calculus was expelled after cystoscopic manipulation.

with multiple catheters, and 12, or 6 per cent, were extracted from the ureteral orifice. In 21 instances surgical intervention was required after manipulative efforts were unsuccessful. In 65 patients, or 32.7 per cent, surgical intervention

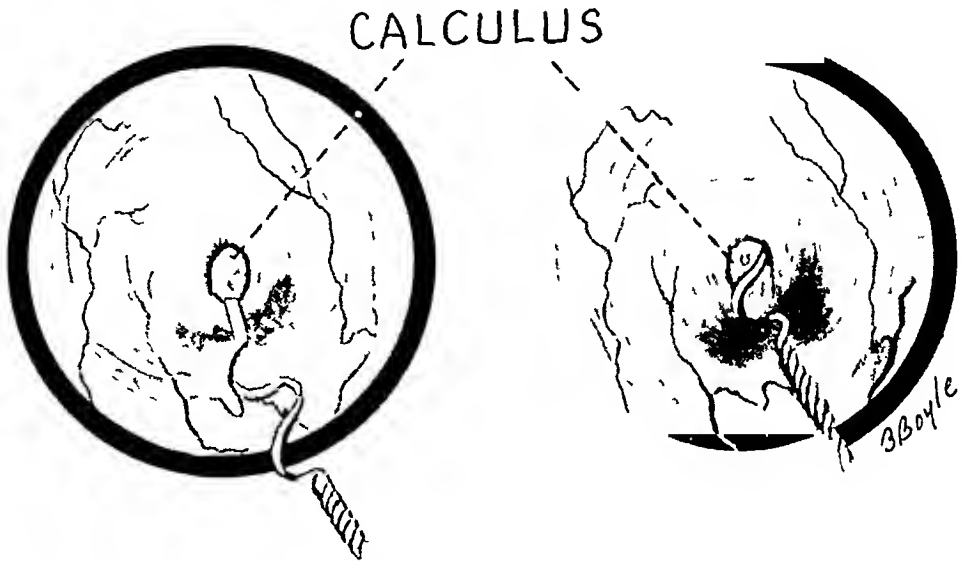


FIG 3—Spiral dislodger for removing stones from the ureteral orifice

was advocated primarily, while in 17 patients operation was recommended but refused by the patient.

In a later series of 251 cases, it was noted that 43, or 17.1 per cent, passed the calculus spontaneously, 171, or 68.4 per cent were removed by surgical intervention, and 37, or 14.7 per cent, were removed by manipulation.



FIG 4—Incision in the lower ureter with cystoscopic scissors, for removal of a stone impacted in the lower end of the ureter

In the present series of 350 cases, 66, or 18.9 per cent, passed the stone spontaneously, in 56, or 16 per cent, the calculus passed after manipulation, while in 228 cases, or 65.1 per cent, surgical intervention was deemed advisable.

From these statistics it is evident that there has been a gradual increase in the number of stones expelled spontaneously or by manipulative procedures.

In a series reviewed by Bumpus and Scholl,⁶ at the Mayo Clinic, 72.7 per cent were removed by open operation, and 27.2 per cent by manipulative procedures.

The high incidence of surgical intervention in the present series may be accounted for by the relatively larger number of stones present in the upper ureter, and the fact that in many instances repeated manipulative procedures had been attempted before the patient entered the clinic, and further manipulative attempts to deliver the stone were not advisable.

In advocating manipulative procedures for the removal of stones from the ureter, the following must be considered. The economic status of the patient, the age of the patient, the size and position of the calculus, coexisting pathology rendering manipulative procedures difficult or hazardous, evidence that the patient does not tolerate cystoscopic procedures such as the development of pyelonephritis following instrumentation, the status of the kidney above the stone, the status of the opposite kidney, a fixed stone or one that has recently passed into the ureter, a stone complicated by a pronounced periureteral reaction usually associated with a fixed stone, in the presence of a progressively enlarging hydronephrosis, with or without infection, when repeated manipulative efforts fail, and certain congenital abnormalities.

Certainly, a dogmatic statement should be avoided as instances may arise in which each of these objections are not tenable.

Surgical Intervention—The operative removal of a calculus from the ureter may constitute but one phase in the management of this group of patients. The status of the kidney above the stone must be given due consideration, as it may be damaged by back pressure and infection to such an extent that its potential ability to repair is nil. If the kidney is pyonephrotic, a nephrectomy is necessary, if a large dilated ureter also is evident, an additional ureterectomy may be advisable. With varying degrees of hydronephrosis conservatism is advisable unless functional studies show irreparable kidney damage.

In many instances the status of the kidney may be determined by intravenous urographic studies, or if a catheter can be passed beyond the stone functional studies and a retrograde pyelogram give the desired information. However, I have seen numerous cases with hydronephrosis associated with ureteral calculi which diminished markedly in size and the function returned to normal, or approximately normal, after removal of the stone. In all instances conservatism is the procedure of choice, if it may be safely recommended.

In recent years, refinement in the operative technic has diminished the period of hospitalization, the mortality, and morbidity in the group of patients in whom ureterolithotomy has been performed. A muscle-splitting operation and an extraperitoneal approach is utilized in removing stones in every portion of the ureter. This lessens the incidence of hernia and in many instances the patient may leave the hospital in seven to nine days after surgical intervention has been instituted.

In removing a calculus from the ureter I prefer to make the incision in the ureter slightly above the point of obstruction rather than directly over the

stone itself. This minimizes trauma to the ureteral tissue overlying the calculus which is already the site of a periureteritis. A forceps is passed gently down to the stone which is easily withdrawn. This decreases the incidence of stricture formation postoperatively.

The incision in the ureteral wall is reapproximated with No. 000 plain catgut sutures, avoiding passing through the mucosa of the ureter. A rubber tissue drain is introduced in all cases.

There is one operative procedure for the removal of a calculus from the lower ureter in women which, I do not believe, has received sufficient attention. This is the employment of vaginal ureterolithotomy. If a calculus can be palpated in the ureter upon vaginal examination, it may be removed readily by this route. This procedure has been employed successfully in 13 patients in this series, with no complications. While it has been stated that a fistula may result, this has not been our experience in any patient in this group.

In the present series of 228 cases, in which surgical intervention was necessary and ureterolithotomy was employed, four deaths occurred. One patient died of peritonitis, one of postoperative pneumonia, one from cardiac failure, and one patient succumbed from a cerebral embolism. In one instance a persistent ureteral fistula occurred, later requiring nephrectomy.

Complications are avoided by adequate preoperative study and postoperative care. The operative procedure *per se* is but one phase in the management of this group of patients. Intensive preoperative study and a well planned postoperative regimen cannot be overemphasized.

CONCLUSIONS

A study of the etiologic factors associated with calculous formation is essential in every patient with a ureteral stone.

A critical evaluation of the procedures available for the removal of a calculus from the ureter must be made in each individual case.

The indications for surgical intervention must not be overlooked and, because of the low mortality and morbidity, should be advised in indicated cases.

Experience with the various procedures available for the removal of a stone from the ureter influences the choice of method or instrument.

The treatment to be recommended is that which, in the experience of the surgeon, has been accompanied by the most satisfactory end-result.

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MALIGNANT TUMORS DEVELOPING IN SACROCOCCYGEAL TERATOMATA

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CONGENITAL MALFORMATIONS and tumors designated as dermoids or teratomata have for centuries greatly impressed and stimulated investigations by many students of biologic and medical problems. The literature dealing with various aspects of the sacrococcygeal group of teratomata alone is so voluminous that no attempt can be made to review it in this paper, nor is it feasible to discuss the various classifications or the theories concerning the nature and embryologic genesis of teratomata. Recent reviews of the subject are those of Ewing,¹ and MacCallum.² The latter presents a detailed and

TABLE I
TEN CASES OF MALIGNANT DEGENERATION OF TERATOMATA
From the Literature

No	Author	Year	Sex	Age at Time of Death	Type of Malignant Tumor	Metastases	Autopsy
<i>Certain Cases</i>							
1	Rudolphy ¹	1897	♀	12 months	Papillary adenocarcinoma	Lungs	Yes
2	Fletcher and Waring ⁵	1900	♂	29 months	Adenocarcinoma	Lymph nodes	Yes
3	Hinterstoisser ⁶	1908	♀	23 months	'Alveolar sarcoma'	Lungs Liver Lymph nodes	Yes
4	Bergmann ⁷	1911	♂	17 months	Papillary adenocarcinoma	Lungs	Yes
5	Stewart, Alter and Craig ⁸	1930	♂	3 years 3 mos	Papillary adenocarcinoma	Lungs Liver Lymph nodes	Yes
6	Renner and Goodsitt ⁹	1935	♀	11 months	Carcinoma	Invasion of rectum	Yes
7	DeVeer and Browder ¹⁰	1937	♂	21 months	Embryonal carcinoma	Lymph nodes	Yes
<i>Probable Cases</i>							
8	Gramm ¹³	1902	♀	21 months	Chondrosarcoma	Lungs Lymph nodes	Yes
9	Pandalai, Forsyth and Stewart ¹¹	1924	♂	12 months	Papillary adenocarcinoma	?	None
10	Susuki ¹	1936	♂	3 years	Adenocarcinoma	Lungs Liver Lymph nodes	Yes

critical discussion of the theories of origin and many references to the original literature are given.

The histologic structure of sacrococcygeal teratomata has been carefully analyzed and described. The unusual nature and behavior of these growths is undoubtedly responsible for the great number of publications, which is entirely out of proportion to the frequency with which these tumors occur.

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Minor variations and insignificant peculiarities are added in some of the case reports of recent date, while other papers are devoted to considerations of the treatment of these tumors. Treatment, indeed, currently represents the major part of the problem of sacrococcygeal teratoma.

Malignant tumors developing in sacrococcygeal teratomata have occasionally been observed. The extreme rarity of such changes and the presence in our files of two cases showing the development of malignancy prompt this report.

An effort has been made to establish the actual number of similar cases in the literature (Table I). Several instances of alleged malignancy, and cited as such, have been omitted from this list on account of insufficient description or apparent faulty interpretation. This refers particularly to cases published in the latter part of the last and early part of this century.

CASE REPORTS

Case 1—History No. H L H 98937. E. E. Y., a white, female baby, was first seen at the age of ten months. She was referred to the hospital by her local doctor with the diagnosis of a tumor of the right buttock. This was present at birth and had slowly increased in size ever since.

Family History—This was negative except for the occurrence of frequent tumors on the maternal side. Both parents are well.

Patient's History—Birth was normal. On the day after birth the mother first noticed that the right buttock was slightly larger than the left. It slowly and progressively increased in size, especially during the eighth and ninth months. The buttock was always firm and at times warm. The anal opening was dislocated toward the vagina. Bowel movements had been quite normal.

Two months ago the child refused to sit or to lie on the right side. The appetite became poor, but there was no loss of weight. A diagnosis of a tumor of the right buttock was made and confirmed roentgenologically. An operation was advised, and the child was transferred to the Harriet Lane Home of the Johns Hopkins Hospital.

Physical Examination—The patient was a ten-months'-old well-developed and well-nourished white female baby, that was extremely irritable and cried when made to sit up or to lie on the back. The baby preferred the knee-chest position and was standing on a wide base. There was marked lordosis. Both buttocks were quite prominent. The right buttock was larger than the left. There was a large, firm and smooth downward-projecting mass in the right buttock. The overlying skin was quite warm and there were dilated veins on the surface. Dilated vessels were also seen in the skin over the lower lumbar spine and the sacrum. There was also some slight yellowish pigmentation of the skin over this area and a mild depression could be seen over the sacral spine which was covered by a slight growth of hair. The sacrum seemed to be pushed backward. The rectum, on digital examination, was found to be pushed over to the left by a smooth, firm, rounded mass in the right side of the pelvis. The posterior vaginal wall was pushed forward slightly into the vaginal cavity. Behind it, a firm mass could be felt in the pelvis. The anal opening was wide and there was prolapse of rectal mucosa. About the anus a ring of bluish discolored skin about 3 cm. in diameter was seen.

The abdomen was somewhat protuberant. No masses could be felt anywhere in the abdomen. A few axillary, cervical and inguinal lymph nodes were palpable but not enlarged. A diagnosis of sacrococcygeal teratoma was made. The roentgenograms confirmed the diagnosis of a large tumor, seemingly arising from the region of the pelvic outlet. Collections of calcium deposits were seen in it. It was thought that these might represent teeth. Laboratory data were negative.

On surgical consultation, it was decided to irradiate the tumor before operation in order to reduce, if possible, the size of the tumor. From October 16, 1936, to November 9, 20 roentgen treatments were given. Half of these were directed to either side of the tumor. The distance was 50 cm, a 2 Mm Cu and a 1 Mm Al filter were used, with 200 K V, 20 Ma, a total of 1,740 r in all was given in the course of this treatment.

The growth of the tumor seemed to come to a standstill, whereas it had been increasing in size before treatment. The patient tolerated these irradiations well. Twice there was a transient diarrhea.

The patient was discharged in good general condition, and was to be followed further in the dispensary. Just before discharge a soft cystic mass was felt at the dividing line between the two buttocks.

About three months later, at 15 months of age, the patient was admitted again. She had had a persistent upper respiratory infection while at home. Otherwise, she had been well until six days before admission, when it was thought that the tumor was growing again. At this time several areas of fluctuation were felt in the tumor, which now involved both buttocks, particularly the right.

During a period of 12 days, nine roentgen treatments were given. The dosages were as follows: 200 KV, 20 Ma, skin-target distance 50 cm, $\frac{1}{2}$ Mm Cu and 1 Mm Al filters. A total of 792 r was delivered. Five irradiations were directed toward the tumor from the left and four from the right side. There was no change in the tumor at that time, and the patient was again discharged for further observation in the Out-Patient Department. The child remained at home for three and one-half months. She received one treatment with radium in the second month (one month previous to her third admission).

Soon after the radium treatment the child became irritable and refused to stand or walk. She looked pale and lost weight. Two weeks before admission she developed obstinate constipation. She was admitted for the third time at the age of 19 months. The tumor had grown considerably larger and two soft lumps of large size had appeared on the surface of the mass. There was more distortion of the rectum and of the genitalia. Both legs were partially paralyzed and the muscles atrophied. In the right lower quadrant of the abdomen there was a firm mass projecting from the right pelvis and extending to the midline.

Operation—June 18, 1937. Under general anesthesia, a large, partially firm and partially soft tumor was shelled out and dissected away from the bladder and the rectum. The tumor was found to extend up into the pelvis and was firmly attached to the coccyx, which was resected. The sacrum was curetted, since the tumor was attached to it also. A nodular mass of tumor was seen to extend up into the abdominal cavity and this could be removed also. The patient stood the operation well, and immediately postoperative had a formed stool. Several transfusions were administered. The operative wound drained and healed slowly.

After an initial improvement during the first three weeks after operation, an abdominal mass could be felt. It extended up to the umbilicus. Small ulcerations appeared about the rectum and the child became more and more cachectic. The abdominal mass increased rapidly in size and the liver became enlarged. The child died two months after the operation, at the age of 21 months.

Autopsy Report (No 15448, Doctor McAllister). The description will be limited to points of particular interest.

The body is that of an extremely emaciated and dehydrated female baby. Many dilated veins are seen over the abdomen and over the back. There are several small shallow ulcers in the perineal region, and there is a draining sinus leading into the right buttock. There are a few palpable lymph nodes in each groin. Both buttocks are enlarged, the right being larger than the left. No other lesions are seen externally.

Gross Pathology—A large tumor mass, situated in the retroperitoneal tissue pushes all the abdominal organs upward and anteriorly, including the aorta, the inferior vena cava,

and both ureters, which overlie this mass. The tumor measures approximately 13×13×2.5 cm. The right ureter is obstructed and the vena cava is dilated distally. The main tumor has eroded the vertebrae and intervertebral disks and the right ileum posteriorly. The tumor is soft, somewhat lobulated, and greyish-yellow. Several cysts are found in the tumor, the largest measuring 2.5 cm in diameter. The tumor surrounds the vena cava and aorta. In the inferior vena cava there is, completely filling the lumen, soft yellowish material.

The entire region of vagina and ureteral orifices is infiltrated by the tumor. There is tumor material in the marrow of the head of the femur.

The large tumor is continuous with a smaller tumor in the right buttock. The draining sinus mentioned earlier, communicates with this mass which is somewhat firmer and pink. The left buttock is free.

Many small nodules are found in both lungs and in the liver. These are of a greyish-white color and soft. The largest ones measure about 1.5 cm in diameter. A mucoid material can be squeezed out of them. A few cystic areas are seen in some of them. Bronchial, periportal and retroperitoneal lymph nodes contain similar gelatinous tumor nodules.

The tumor removed at operation measures 12×10.5×10 cm. It is somewhat pear-shaped and surrounded by, for the most part, a smooth fibrous capsule. Portions of fat, numerous adhesions and remains of muscle are seen on one side. The opposite side of the tumor is smaller. It is on this part of the tumor that most of the adhesions and muscle tissue are found, and it shall be referred to as the base. The tumor is rather soft and of a somewhat elastic consistency. When cut in numerous sections, the surfaces present a rather uniform picture—showing numerous cysts varying from a few millimeters to 3.5 cm in diameter. Most of the cysts are thin-walled and transparent. Many contain a gelatinous tenacious bluish-grey opaque material. Groups of cysts are sometimes surrounded by a membrane of connective tissue, giving it a nodular appearance. Small areas of black pigmentation are occasionally seen in the tumor. A few calcified foci are encountered, but no teeth are found. The capsule of the mass varies in thickness from 3 to 1 cm. At the base and along one side of the tumor there is a slit-like separation of the capsule, dividing it into a parietal and visceral portion. The narrow elongated cavity contains a small amount of greasy material and a few hairs in places. The inner surface of this cavity is roughened here and there. The more solid tissue at the base shows some large areas of necrotic, friable material in close association with some of the cystic cavities.

Microscopic Examination—The tumor removed at operation shows a dense partially hyalin capsule and a variety of tissues. There are derivatives of all three germ layers. The cysts are lined by ciliated and nonciliated cylindrical epithelium, resembling the mucosa of trachea. Some cysts are lined by squamous epithelium. Islands of squamous cells are often found in the cylindrical epithelium as well. Other cysts are lined by cuboidal or flat epithelium. Many mucous glands, with ducts, are present in the interstitial tissue. The lumina of many cysts are filled with a homogeneous somewhat pink-staining material. In addition, parts of the following structures are found in the tumor: Cartilage and bone, smooth muscle, pigment cells, intestinal mucosa, pancreas with islands of Langerhans, ovarian stroma with structures resembling follicles, choroid plexus, nervous tissue, epidermal epithelium with appendages. There are inflammatory cells in some parts of the tumor, and a sinus is found showing fresh granulation tissue in which a few giant cells are seen.

Sections from the base of the tumor show an entirely different type of tissue in addition to the above-mentioned structures. It is composed wholly of a single-type of cell which has large polygonal and relatively pale-staining nuclei with little chromatin and but scant cytoplasm. In some regions the cytoplasm of the tumor cells is vacuolated. The cells grow in single layers or in massed sheets. They are situated on a delicate vascularized network of connective tissue. Numerous papillary proliferations are seen and the tissue has, on the whole, the characteristic appearance of a papillomatous tumor. In some

areas an acinar structure is noted. Here a pink-staining, homogeneous material is often found in the lumina, formed by the tumor cells.

The number of mitotic figures varies considerably. In focal areas tumor cells are compactly clustered and in other areas the structure is loose. There are foci of necrosis and hemorrhage. There is invasion of adjacent tissues and blood vessels.

It is this tumor which has invaded the bones and retroperitoneal tissues. There is a thrombus of tumor cells in a branch of the left external iliac vein. The metastases in the liver and lung show the same type of tumor cell. Other microscopic studies revealed a chronic cystitis and an acute necrotizing pyelitis of the right kidney.

Anatomic Diagnosis. Congenital coccygeal teratoma, involving right buttock. Papillary adenocarcinoma arising in teratoma and invading right buttock, lower lumbar and sacral vertebrae, right ileum and head of femur. Extension of tumor into pelvic and retroperitoneal tissues. Metastases in liver, lungs, retroperitoneal and bronchial lymph nodes. Urethral and ureteral obstruction by tumor. Chronic cystitis. Chronic and acute necrotizing pyelitis, right. Compression and invasion of pelvic veins and inferior vena cava. Draining sinus communicating with tumor mass in right buttock. History of preoperative roentgenotherapy and radium treatment.

Case 2—History No 3822. H. E. B., white, male, age 13 months, was admitted to the Johns Hopkins Hospital, April 12, 1926, because of constipation and anuria.

Family History—Not remarkable.

Patient's History—Patient was a full-term child. At the time of birth a small reddish discoloration was noticed just to the left of the coccyx on the thigh. This resembled a birth mark. It measured about 1.5 cm in diameter. The family physician advised no treatment. At the age of two or three months a small lump of walnut-size was found in addition to the discoloration. Neither the discoloration nor the lump seemed to increase in size during the first four or five months of life. A little later the mother thought that the area of discoloration and the mass beneath it increased in size. The attention of the family physician was called to this but he advised against any interference. The child developed some slight constipation at the age of about nine months. Since the child was given solid food for the first time during this period, it was thought that the constipation was due to the change of food. The constipation persisted, however, and became worse slowly, so that at the age of 12 months, enemas had to be given. A doctor was again consulted and he gave calomel, whereupon the bowels moved freely, though for a short time only.

A week later it was noted that the left leg was somewhat swollen. The area of discoloration and the mass beneath were larger than before, and there were dilated blood vessels in the skin above and around it. The child lately assumed a knee-chest position when awake and seemed to be much more comfortable in this position.

One week before admission, at the age 13 months, the child seemed toxic and was passing very small amounts of urine. Catheterization was performed, and the child was relieved. Repeated catheterization became necessary, which procedure became more and more difficult. As the symptoms of constipation and anuria became worse, and catheterization more difficult, it was decided to hospitalize the child.

When the patient entered the hospital he had not voided for several hours, and the bladder was greatly distended. A retention catheter was introduced and a decompression apparatus used. The retention was relieved, and the child started voiding again in about one week.

Physical Examination—The patient was a slightly under-developed, weak and irritable child. The abdomen was distended. The bladder dulness extended two fingers' breadth below the umbilicus. On the left buttock, to the left, and close to the sacrum and coccyx, there was a subcutaneous, soft mass covered by bluish discolored skin, measuring about 3 cm in diameter. It was freely movable, but seemed to be attached to the deeper structures of the sacrum. The superficial veins of the skin were dilated. The left thigh was swollen. On suprapubic palpation an indefinite mass could be felt along-

side the distended bladder. On rectal examination an almost complete obstruction of the rectum was found in the ampulla. A slit-like opening was all that remained of the rectal canal. The rectal mucosa was smooth and intact everywhere. A large tumor mass could be felt, this was firm and filled out the concavity of the sacrum and was attached to both sides of the pelvis. The mass was so firm as to suggest bone formation. Roentgenologically, a distortion of the lower portion of the sacrum was noticed.

A diagnosis of tumor of the pelvis was made, with the probability of a periosteal sarcoma. Hence, roentgen and radium treatment seemed most advisable. This combined treatment was carried out during the following weeks. The roentgenotherapy was continued for 18 days, beginning at a dosage of 15 minutes and gradually increasing up to 20 minutes. He was given a total of five half-hour radium treatments per rectum, making a total of 500 mc. hours.

A few days after entering the hospital the left thigh was noticed to be swollen and there was definite swelling of the left inguinal nodes. The right inguinal nodes were normal in size.

The treatment was well-tolerated, and the tumor mass became much smaller. The intestinal and urinary obstruction disappeared almost completely. The patient was able to void and normal stools were passed. The swelling of the left thigh and the discoloration of the skin had disappeared, and the subjacent tumor mass had decreased to about one-half the size noted on admission. The patient was discharged 19 days after admission.

For two weeks, roentgenotherapy was continued three times a week. The child improved steadily and continued to do well for about one month. Re-examination, in about four weeks after discharge from the hospital, showed a fairly well-nourished child. An indefinite mass could still be felt on palpation to the left of the midline in the pelvis. The mass had decreased in size considerably. The enlarged lymph node in the left groin had entirely disappeared. The left thigh was still a little larger than the right. The mass in the upper portion of the left buttock was still present but it was much smaller and softer than before.

The general improvement of the child lasted for about one month. After this time the tumor began to grow rapidly. Urinary obstruction occurred again.

On June 1, 1926, two months after the final admission, the tumor had spread to the inguinal nodes on the left side and also the right side. Small nodular masses could be felt in the abdomen and in the liver. The tumor at the coccyx had not increased in size. Roentgenograms showed metastases also in the lungs. The child became weaker, and finally died, July 26, 1926, almost four months after the final admission.

Autopsy Report (No. 9375, Doctor Forbus). The report will be limited to the points of interest (Abdominal incision only).

The body is that of an emaciated male child, 16 months of age. The abdomen is greatly swollen. The lower extremities are edematous, the left leg more so than the right. Both buttocks are quite prominent. Just to the left of the tip of the coccyx, and extending for about 5 cm. up over the posterior surface of the sacrum, there is a soft cyst-like mass. The overlying skin is of a bluish color.

The abdominal organs are greatly distorted in shape and location, due to the presence of extensive nodular masses. In the pelvis, occupying the retroperitoneal tissues, there is a large tumor mass which completely fills the whole cavity. This has pushed aside all the pelvic organs. The bladder is pushed far upward, in such a way that it rests on the anterior surface of the tumor mass, right above the brim of the pelvis. In attempting to remove the tumor, after a dissection of the pelvic organs which are not involved by it, it is found that there is a direct continuation of tumor tissue into the structures of the left thigh beneath the inguinal ligament. The tumor is very densely attached to the floor of the pelvis and to the anterior surface of the sacrum and coccyx. There is no invasion of any bony structures. There is a distinct continuity between this tumor and the cystic tumor which was described as being located in the sacral region externally. It is easy to remove the sacral cystic tumor from its bed.

The branches of the vena cava inferior are markedly compressed by tumor masses and a thrombus is found in the main stem of the inferior vena cava. There is an ulceration of the mucosa of the rectum. The retroperitoneal tissues and lymph nodes are diffusely invaded and replaced by a rather soft yellowish-grey, brittle tissue which is of a tenacious and mucinous character. There are widespread hemorrhages. There are numerous metastases in the liver, the lungs, and in bronchial lymph nodes. The better preserved, smaller metastases show a homogeneous grey, granular surface with some mucoid material. There is tumor tissue in branches of the portal veins also.

The pelvis of each kidney is somewhat dilated but there is no appreciable dilatation of the ureters. The other organs show no lesions.

Frozen-section of the sacral tumor shows a variety of tissues including intestinal mucosa, skin, and nervous tissue. Sections of the invading tumor show a different type of tissue, which will be described later.

The sections which remain for study (other sections and blocks have unfortunately been lost) show the following. The tumor mass, located subcutaneously in the left buttock, shows a single cyst lined by squamous epithelium. Sections from the cystic part of the pelvic tumor show cysts lined by high columnar mucus-producing epithelium. The epithelium sometimes changes in character from place to place. In some places it is squamous, in others ciliated, in again others it is cuboidal. A few hair follicles are seen in the cysts lined by squamous epithelium. These cysts are surrounded by a rather dense connective tissue. An island of undifferentiated epithelial tissue is found in the interstitial tissue. Smooth muscle as well as nervous tissue is seen.

The malignant tumor is composed of different cells. These cells are somewhat cuboidal, they have little cytoplasm and consist for the most part of large polygonal nuclei with varying amounts of chromatin. The nuclei are relatively pale. These tumor cells are arranged in various ways. They tend to grow in single layers along fine strands of connective tissue, forming small papillary branching structures. In other places they grow in solid columns and in others small acini are formed by tumor cells. Solid nodules of tumor cells are found here and there, surrounded by connective tissue membranes. A cystic appearance is frequently seen and in these parts a pale bluish, homogeneous substance lies between loosely arranged tumor cells. Many mitotic figures are seen. There are necroses and hemorrhages. The metastases throughout the body show the same type of cell and the same variations in arrangement, which is predominantly that of a papillary adenocarcinoma.

The remaining organs show no lesions except for a chronic ulceration of the mucosa of the rectum, which shows loss of mucosa and granulation tissue with an occasional giant cell.

Anatomic Diagnosis. Papillary adenocarcinoma arising in cystic sacrococcygeal teratoma. Extension of tumor into pelvic and retroperitoneal tissues and left thigh. Metastases in liver and lungs, retroperitoneal and bronchial lymph nodes. History of repeated urinary and intestinal obstruction by pelvic tumor and of deep roentgen and radium treatment with relief of symptoms. Pigmentation of skin. Ulceration of rectum. Slight obstruction of both ureters and slight hydronephrosis, bilateral. Thrombosis of inferior vena cava.

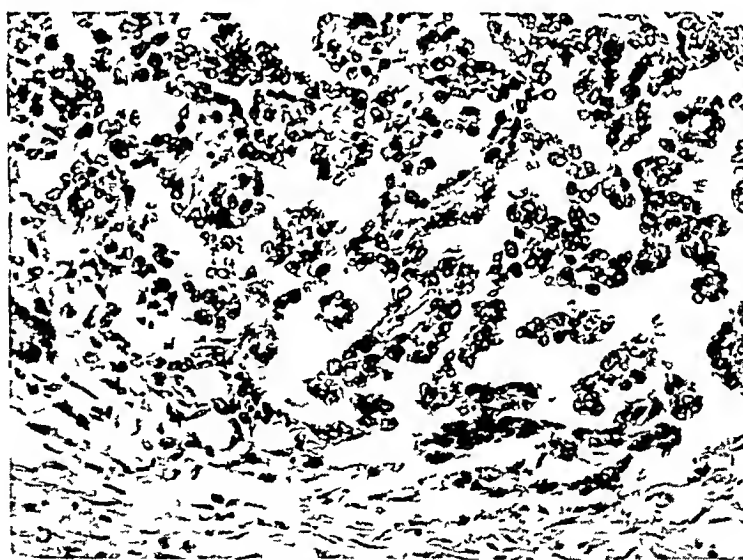
DISCUSSION—Both cases represent typical congenital sacrococcygeal teratomata. They were both found at, or soon after birth. Derivatives of all three germ layers were found in both tumors.

The outstanding feature in these two cases is the development of a malignant tumor in the teratoma. Both tumors had infiltrated the adjacent tissues and metastasized to various organs. They showed very striking similarities in structure (Figs 1 and 2).

It has been pointed out by several authors that teratomata—wherever

they occur—are a potential source for the origin of a malignant tumor. MacCallum² states “While it is true that the teratoma itself is benign, it is not at all uncommon to find the development of a distinct carcinoma at some point in its epithelium, exactly as we find it in the body in general.” As a rule, one type of cell only assumes the malignant character and spreads throughout the body. The possibility that a variety of cells in a teratoma are stirred to such

A



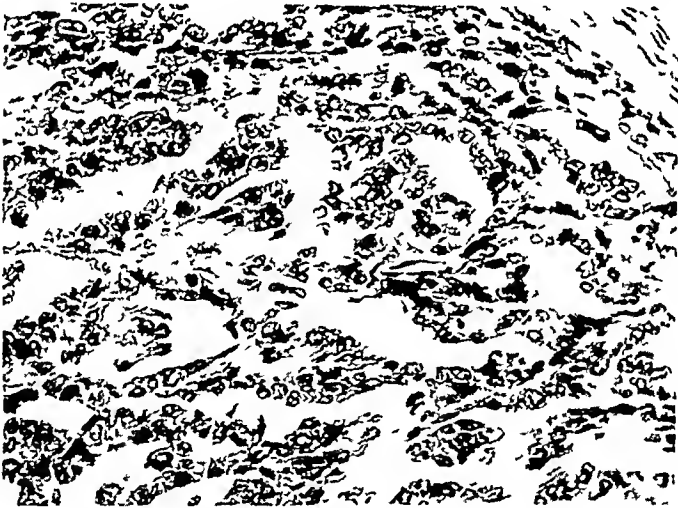
B

FIG 1—Case 1 Path No 15448 (A) Portion of teratoma (B) Portion of papillary adenocarcinoma

a change and that combinations of tissue metastasize is remote, and has not been shown to occur. However, Schaefer³ reports a remarkable case of a 14-year-old girl who had a teratoma of the left ovary. This was composed of mature and immature tissue elements of all three germ layers. In addition, a very immature and unclassifiable type of tissue was seen in it. There were numerous metastases and in these all tissues of the original tumor were found. The immature cell-forms predominated in the metastases. As it is unlikely

that tissue complexes became malignant and metastasized, as pointed out above, the author explains his case by assuming that a part of the very undifferentiated multipotential portion of the teratoma became malignant. These cells were then swept away by either the blood or lymph stream or implanted themselves on the peritoneum. Here, a number of them proceeded to differentiate and thus images of the original tumors were formed, containing

A



B

FIG 2—Case 2 Path No 9375 (A) Portion of teratoma (B)
Portion of papillary adenocarcinoma
(Photographs by Milton Nongl)

cysts, cartilage, and neuro-ectodermal tissues. It seems likely that in this case also only one type of cell was stimulated to malignant growth.

The cases reported herewith, and all those collected from the literature showed the development of malignancy, also, of only one type of cell. It is interesting, in this connection, to note the frequency of papillomatous adenocarcinomata. Moreover, all but two cases were malignant tumors of epithelial origin. The case of Hinterstoisser⁶ can probably be interpreted, on account of

the minute description, as a carcinoma, while the exact nature of the tumor described by Giamm¹³ remains obscure

The first trustworthy report of a malignant tumor arising in a sacrococcygeal teratoma is that of Rudolph⁴. The description of the original tumor, undoubtedly, characterizes it as a teratoma and the detailed report on the histology of the malignant tumor makes the diagnosis of a papillary adenocarcinoma certain. The case of Fletcher and Waring⁵ also seems to be beyond doubt, judging from the clinical and pathologic data. In Hinterstoisser's⁶ case a teratoma was described containing cystic cavities, bone and cartilage, and also some structures which were referred to as round cell sarcoma. The child was well for 21 months after operation, and then a pelvic tumor was found. At autopsy there was a large retroperitoneal mass with metastases in lymph nodes, lungs and liver. This was diagnosed as large cell alveolar sarcoma. It is likely, and the description suggests, that the author was dealing with an adenocarcinoma, although its identity cannot be ascertained today. The case of Beigmann⁷ (No. 4 of his series) undoubtedly belongs in this series. No malignant changes were found in the teratoma removed at operation but four and one-half months later a large pelvic and retroperitoneal tumor and widespread metastases were found at autopsy. The tumor showed a papillary structure and gland formation. The case of Stewart, Alter and Craig⁸ is a typical congenital sacrococcygeal teratoma in which a papillary adenocarcinoma developed. There were metastases in liver, lungs and lymph nodes. In Renner and Goodsitt's⁹ case a typical postsacral teratoma was found and removed at operation. Ten and one-half months later a second tumor had developed which was anterior to the sacrum. Both proved to be teratomata, but in the second tumor a papillary tumor with attempts to gland formation was described in addition to the teratomatous structure. There was invasion of the wall of the rectum. DeVeer and Browder¹⁰ describe a sacrococcygeal teratoma in a six-months-old child. This was removed and no malignant changes were found. Fifteen months later the child died of a tumor, with local extension and metastases to lymph nodes. The tumor is described as embryonal carcinoma.

To these seven cases three more can be added, although they do not show as much evidence either of the true nature of the teratoma or of the malignant tumor.

The case of Pandolai, Foisyth and Stewart¹¹ is another example of a papillary adenocarcinoma, developing in a teratoma. The papillary adenoma and carcinoma are supposed to have shown striking resemblances to tumors of the choioid plexus. There was no autopsy. Susuki¹² in a paper on "Teratomata" describes an adenocarcinoma with widespread metastases originating in the left buttock. He fails to describe the teratoma. The clinical history is suggestive of the presence originally of a congenital teratoma. The case of Giamm¹³ has been noted frequently as an example of this type of tumor. As the original paper was not obtainable it is impossible to include this case with any degree of certainty in this series. However, the data given

in other papers^{6, 14} do indicate that there was a teratoma, and do suggest that there was a malignant tumor with metastases to the lungs and lymph nodes. It was diagnosed as chondrosarcoma.

Additional cases described as teratomata with malignancy and some of them cited as such as in the literature, are those of Frank,¹⁵ Nakayama,¹⁶ Leopold and Phillips,¹⁷ Heigl,¹⁸ Sawday,¹⁹ Weintraub and Young,²⁰ and Gruber.²¹ These cases have been referred to in an earlier paragraph and it may suffice to say that there seems no justification to include these cases in this list. There was either apparent misinterpretation of the nature of the malignant tumor or absence of any evidence of a teratomatous tumor. Metastases occurred in none of them, and some of the reports are too fragmentary to draw any conclusions (Table I).

COMMENTS—It is well known that malignant tumors may arise in teratomata in other parts of the body. They occur, for instance, in such tumors of the testis, the ovary, or the mediastinum. The material presented in this paper clearly demonstrates the possibility of malignant degeneration in the group of sacrococcygeal teratomata. This potential danger should be borne in mind in all consideration of treatment. Law,²² in a discussion of pelvic tumors with sacral attachments, advocates early treatment. "We believe that, owing to the demonstrated tendency to malignant degeneration, these tumors should be removed when recognized." Similar opinions have been voiced by Stewart, Alter and Craig,⁸ and others. Irradiation as a palliative measure is undoubtedly indicated in all cases in which malignancy with metastases has ensued. The demonstrated recurrence in some cases and the development of malignancy even after early operation perhaps indicates the necessity of postoperative prophylactic irradiation even in the absence of malignant changes in the tumors removed at operation. Since some of the malignant tumors were found in the tissues at the base of these tumors (near the point of attachment to bone, connective tissue, or cartilage) it appears important to pay particular attention to this region in microscopic studies of operative specimens.

SUMMARY

(1) Two cases of typical congenital sacrococcygeal teratoma are reported. In each of them a papillary adenocarcinoma with widespread metastases developed.

(2) The literature is reviewed and ten similar cases have been found.

(3) The necessity of early surgical treatment is pointed out.

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STUDIES ON THE BLOOD HISTAMINE IN CASES OF BURNS*†

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ALTHOUGH a great amount of experimental work and clinical observation has been directed toward the solution of the etiology of shock in general, there still remains a divergence of opinion as to the actual factor or factors which may be responsible. Perhaps, as Blalock¹ notes in his recent monograph, there is more evidence in favor of the toxic theory in burn shock than in most other forms. This is borne out in part by the results of treatment which inhibits the absorption of toxins, such as the tannic acid method of Davidson².

The possibility that some toxin might be liberated from burned tissue, and thus be responsible for the shock-like state which is sometimes observed in patients after burns, was considered early in the studies on this subject, and a great many possible agents have been named. Evidence in favor of the toxic theory is based mainly on the effect of transplanting the skin of burned to healthy animals, producing shock in the recipients and alleviating symptoms in the donor animals (Vogt,³ Vaccarezza⁴), or on the effects of the injection of extracts from burned tissues into healthy animals (Robertson and Boyd⁵), or in the detection of a vasodepressor substance in the fluid perfusing a burned limb (Nagamitsu⁶). Much of this work, however, has remained unconfirmed, and evidence against the toxic theory of burns has been presented by Harrison and Blalock⁷ who were unable to note any effect on animals due to the transplantation of burned skin. Further evidence against this theory was provided by Harkins, Wilson and Stewart,⁸ and Fender.⁹ An excellent review and discussion has been given by Harkins.¹⁰

In the early experiments on histamine, Dale and Laidlaw¹¹ noted the marked similarity between the effects of a large dose of histamine and the symptoms of traumatic shock. They suggested that the absorption of histamine or some similar substance might be the cause of the symptoms of traumatic shock. As pointed out by Barsoum and Gaddum,¹² there is a marked similarity between the electrolyte and other changes of the blood in both conditions. Subsequent investigation, however, did not support this theory, principally because of the inability to demonstrate an accumulation of histamine in the blood of shocked animals (Smith¹³). Furthermore, the experiments of Dragstedt and Mead¹⁴ showed that when histamine shock was produced in

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dogs, histamine could readily be found in the blood of these animals. On the other hand, using the same methods of detection, it was not possible to note an increase of the histamine content of the blood of dogs in traumatic shock. Thus, the histamine theory of shock was rejected by many workers, for it was thought that if histamine were responsible for the production of symptoms, it must be increased in the peripheral blood. As will be pointed out, this conception may be an erroneous one in the case of the human at least.

The first observations on the blood histamine after burns were made by Barsoum and Gaddum¹² shortly after their description of the method for the extraction of histamine in blood. Nine cases in all were investigated, four of which were described in detail. A marked increase in the blood histamine was noted after the fifth or sixth day following the burn, later than the usual time for the development of secondary shock. They felt, however, that there was some correlation between the area of the burn and the magnitude and duration of the rise in histamine but were of the opinion that there was no clear evidence of a correlation between the blood histamine and the clinical condition of the patient. Code and MacDonald¹⁵ described an additional case of burns in whom the blood histamine was determined. Their findings agreed, in general, with those of Barsoum and Gaddum¹².

In the present studies, seven cases were available. Six of these were burned at the same time, and three were admitted to the Royal Victoria Hospital within an hour of the accident. Three others were admitted to the Montreal General Hospital, and were not studied until the ninth day. A seventh case, previously described (Rose and Browne¹⁶) is included.

In all instances the histamine content of the blood was determined by the Code¹⁷ modification of the Barsoum and Gaddum¹⁸ method. Hemoglobin estimations were carried out using the Evelyn photo-electric colorimeter, and the plasma proteins were determined by the falling-drop apparatus, as recommended by Scudder¹⁹. Blood specimens were removed from the large vein on the outer aspect of the arm or from the antecubital vein when possible. Stasis was avoided by the removal of the tourniquet before withdrawing the blood and clotting was prevented by the placing of a small amount of heparin (Connaught Laboratories) in the syringes. In this manner, all the determinations could be made from the same specimen of blood. Hematocrit estimations were always carried out as an additional check on the hemoglobin, and as a means of obtaining the small amount of plasma necessary for the determination of the plasma proteins. All histamine determinations are expressed as *gamma* of base per 100 cc of blood (*gamma*, or $\gamma = 0.001$ mg, or microgram).

Blood Histamine in Normal Patients—In a previous communication (Rose and Browne¹⁶), histamine determinations were carried out on the blood of 50 normal persons. It was found the average histamine content of the blood is 4 γ per 100 cc with variations of from 2–7.5 γ per 100 cc. It was noted, further, that the histamine level of the blood of any one individual remains remarkably constant over long periods of time. These findings agree, in general, with those of Barsoum and Gaddum,¹⁸ and Code and MacDonald.¹⁵

EFFECT OF CUTANEOUS BURNS ON THE BLOOD HISTAMINE OF PATIENTS

Case 1—Patient No 289 This man was admitted to the hospital within one hour after sustaining severe burns about the face and neck, both hands and forearms, and the area about the elbows. His condition was considered fair. A specimen of blood was obtained and, under a general anesthesia, his wounds were cleansed and tannic acid was applied. He received an intravenous injection of 500 cc of half plasma and saline. The details of treatment, along with the changes in the blood histamine, hemoglobin, plasma proteins and blood pressure are shown in Chart 1. It will be observed that there

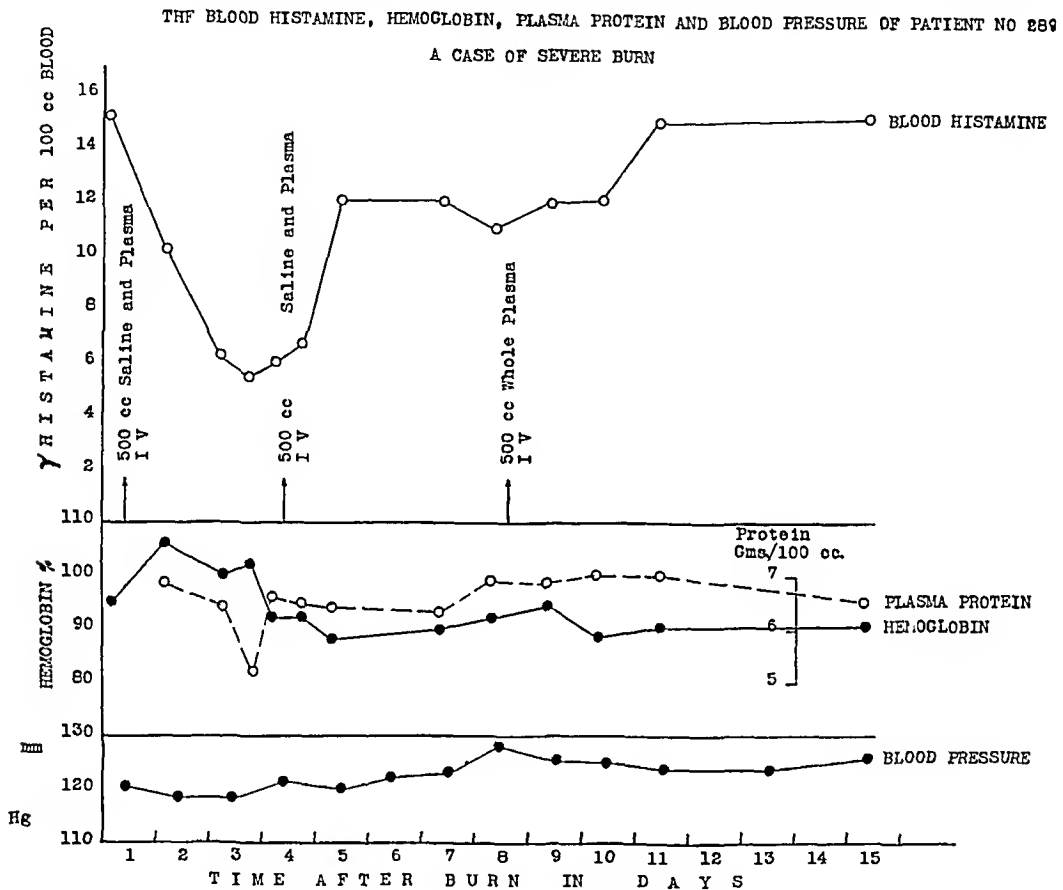


CHART 1—Case 1 The blood histamine, plasma protein, hemoglobin and blood pressure are shown

was little alteration in the hemoglobin and plasma protein, indicating that the intravenous therapy was adequate, and that hemoconcentration was being controlled. The blood histamine was high one hour after the burn, and it will be noticed that there was no indication of shock at this time. The blood histamine fell rapidly to a level of about 6γ per 100 cc on the morning of the third day, where it remained for several days. At this time there was a moderate amount of edema, but the clinical condition of the patient was good. It will be noticed that there was a slight tendency to hemoconcentration at this time also. On the fifth day, as the patient began to improve clinically, the blood histamine had risen to a high level, reaching 15γ per 100 cc on the eleventh day, where it remained until the twentieth day, when he was discharged.

Case 2—Patient No 290 A male, age 27, was admitted to the hospital one hour after sustaining very severe burns about the head, face and neck, upper chest and back, both hands, forearms and lower arms. His condition was considered to be serious and it was believed that part of the upper respiratory tract mucous membrane was also

damaged. A sample of blood was taken and, under a general anesthesia, the wounds were cleansed and tannic acid was applied. An intravenous injection of 500 cc half plasma and saline was administered. On the following morning, there was beginning evidence of edema, and the patient was slightly toxic. Because the hemoglobin had risen to 114 per cent an intravenous injection of 1,000 cc half saline and plasma was administered. Blood concentration was adequately controlled by the intravenous administration of plasma from this time, as indicated in Chart 2. Clinically, however, the patient was very

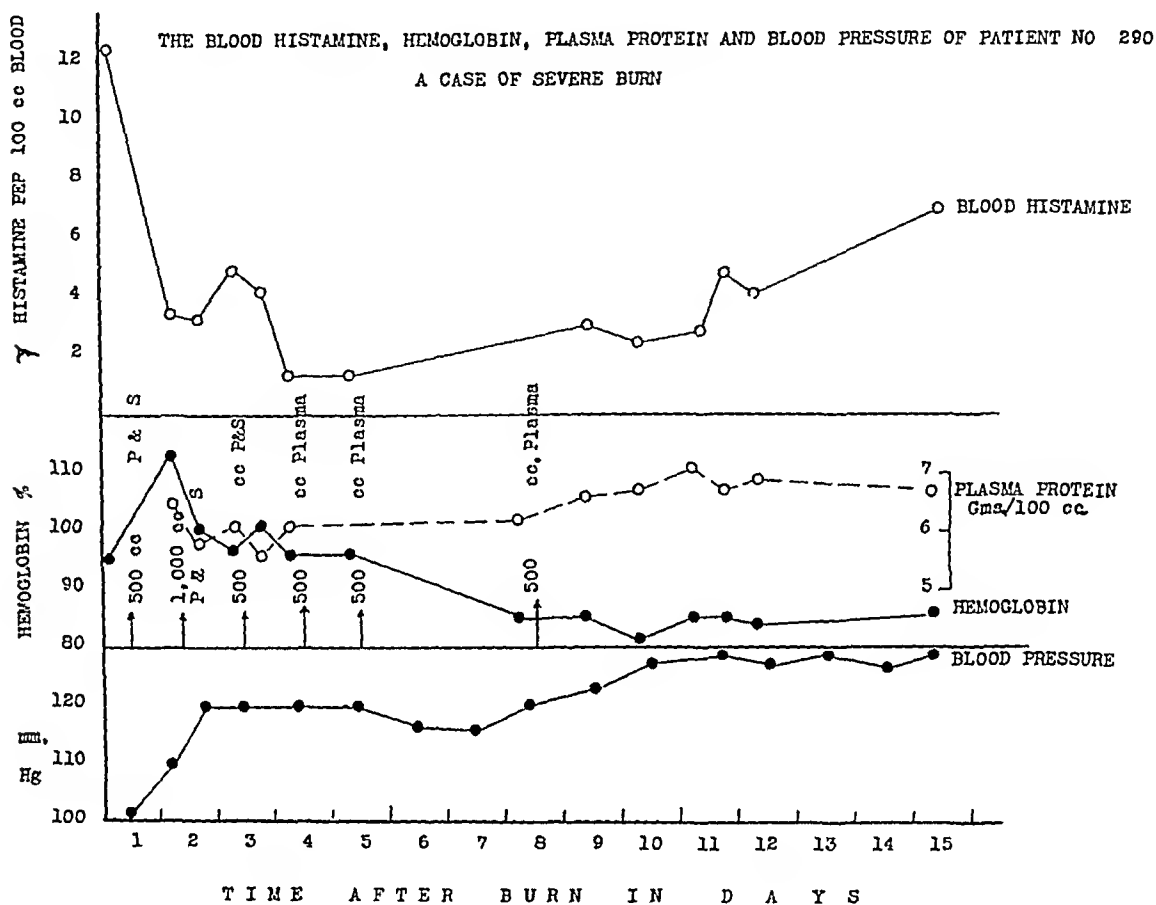


CHART 2—Case 2 The blood histamine, plasma protein, hemoglobin and blood pressure are shown

toxic and difficult to handle. The edema was very marked about the face and arms, beginning about 24 hours after the burn and increasing until the third day. It began to decrease about the seventh day and he improved slowly from that time on. It will be observed that as the toxemia and edema increased, the blood histamine declined until it was 1.57 per 100 cc on the morning of the fourth day. It was impossible to obtain blood on the sixth and seventh days. It will be seen that there is a definite correlation between the clinical condition and the histamine level of the blood. By the fifteenth day, the blood histamine had reached a level of 6.57 per 100 cc and the patient was discharged on the twenty-fifth day.

Case 3—Patient No 291. A male, age 45, was admitted to the hospital one hour after sustaining severe burns about the face, neck, both hands and the lower forearms. A specimen of blood was taken, and without anesthesia, the wounds were cleansed and saline dressings applied. His condition was considered good. On the following morning, although 2,700 cc of fluid had been taken by mouth, the hemoglobin had risen to 130 per cent, indicating a marked reduction in plasma volume. The details are shown in Chart 3. He was given an additional 1,500 cc of fluid by mouth during the day, and at 11 P.M. the hemoglobin had risen even further, to 138 per cent, and the hematocrit was 80. Thus, though the patient seemed in good condition clinically, marked hemoconcentration had

taken place. He was given 1,000 cc of saline and plasma intravenously, and on the following morning (third day) the hemoglobin was still 118 per cent. By the administration of additional plasma it will be seen that the blood concentration was restored to within normal limits only by the evening of the fourth day. It will, furthermore, be noted that the blood histamine was not greatly increased to start with and fell rather rapidly after the third day to a very low level, 0.57 per cent 100 cc by the morning of the fifth day. Up to this time, the patient had been well clinically, although there was

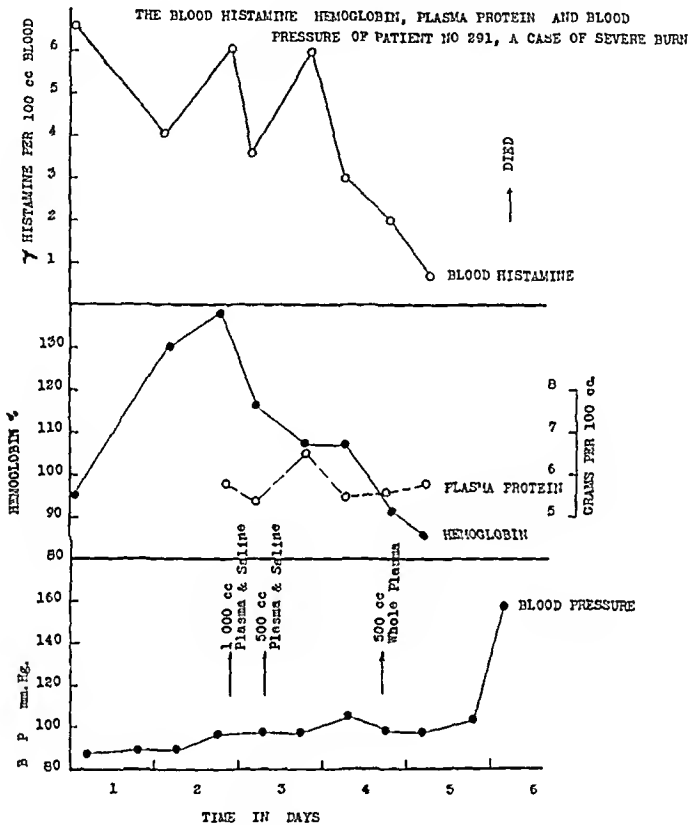


CHART 3—Case 3 The blood histamine, plasma protein, hemoglobin and blood pressure are shown

some purulent discharge on the dressings. About 6 P.M. on the fifth day, he complained of feeling chilly, the temperature and pulse began to increase but the respirations were normal. At about 12:30 A.M. on the sixth day there was a sudden increase in the blood pressure from 100 to 160 mm Hg. The temperature was 105° F and the pulse was about 140. He died suddenly at 2 A.M.

A postmortem examination was made 48 hours later. The burned areas were a bright red. The abdominal viscera appeared slightly pale. The liver, spleen and kidneys were normal in size and appearance. They did not drip blood on section. There was no evidence of ulceration throughout the gastro-intestinal tract. The adrenal glands showed no evidence of gross change and were of normal size. The heart and lungs were removed together. No evidence of a thrombus or embolus was found. The lungs were slightly hemorrhagic. Examination of the brain showed a small brown area about the size of a small pea in the pons. On microscopic section, however, this was found to be due to a localized dilatation of blood vessels and there was no actual hemorrhage. The cause of death was, therefore, not ascertained.

It was previously believed that a midbrain hemorrhage could be the cause of such a

death, but no such lesion was found. Thus, the only abnormal finding which was detectable 12 hours before death was the markedly diminished blood histamine.

Case 4—A male, age 34, was admitted to the Montreal General Hospital with first degree burns about the face, neck and hands. There was also a small burned area on the left leg. Under a general anesthesia, his wounds were dressed with tannic acid and silver nitrate. His condition was good and he made a rapid recovery, being discharged on the fourteenth day. As will be noted in Chart 4 the blood histamine on the ninth and twelfth days was within normal limits.

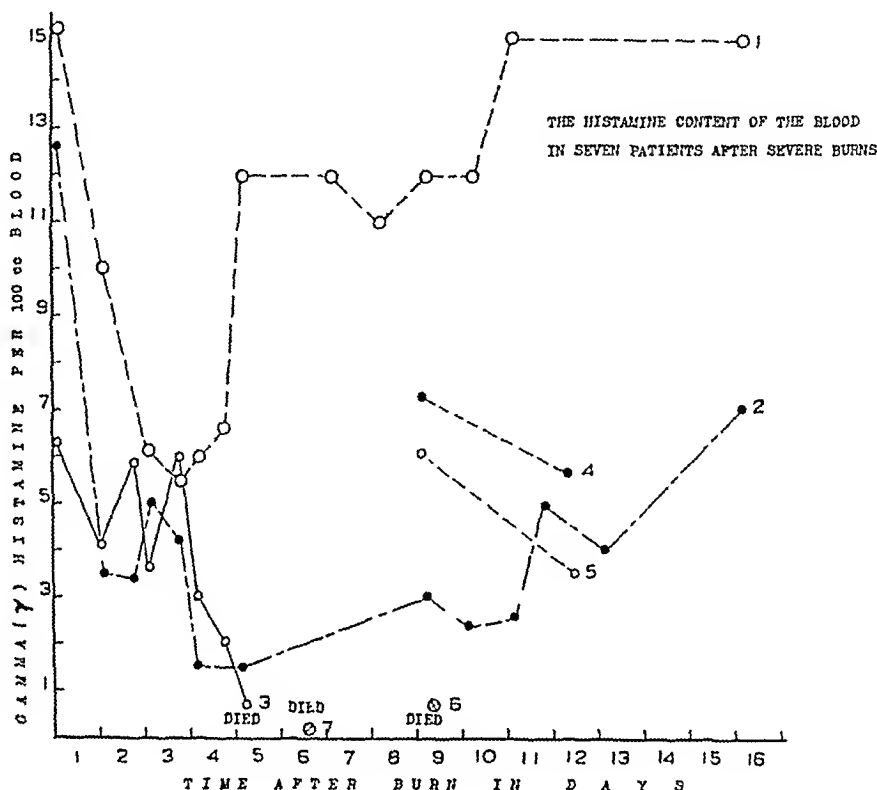


CHART 4.—This figure represents the histamine content of the blood of some cases of severe burns taken at various intervals. It will be noted that immediately following the burn the blood histamine is markedly increased in Cases 1 and 2. There is then a decrease in the blood histamine content of Cases 1, 2, and 3 at about the third and fourth days. This decrease is correlated with the signs of damage and the presence of edema. The blood histamine then decreases even further if the state becomes more severe, as in Cases 6 and 7, or increases as recovery ensues, as will be noted in Cases 1 and 2.

Case 5—A male, age 45, was admitted to the Montreal General Hospital after sustaining third degree burns of the head, face, neck, both hands, wrists, forearms and two-thirds of the back. The burned areas were sprayed with gentian violet. The hematocrit reading was 54 on the day of admission and 61 on the second day. Histamine determinations were made on the ninth, twelfth and sixteenth days. It will be seen (Chart 4) that they were within normal limits. The hematocrit readings were 41, 41 and 39, respectively. He made a good recovery.

Case 6—A male, age 34, was admitted to the Montreal General Hospital with first and second degree burns about the head, face, neck, left side of thorax, hands and forearms. Under a general anesthesia, tannic acid and silver nitrate were applied to the wounds. The urine contained albumin on the third day, and R. B. C. and casts appeared by the fifth. Anuria developed on the ninth day. The blood histamine was determined on the ninth day, and was found to be markedly decreased. The hemoglobin was 106 per cent, and the hematocrit was 48 (Chart 4). A transfusion of 500 cc. was given on the tenth day, and on the following day he died.

Case 7—Patient No. 86. A female, age 45, was admitted to the Royal Victoria

Hospital following severe burns to the chest and abdomen. The wounds were cleansed and tannic acid was applied. She was not seen until the sixth day, when a blood specimen was obtained. No histamine was found in the blood and the patient died on the following day. There was no autopsy.

Discussion—From a survey of the results obtained in the present studies, it will be observed that following severe burns, changes in the blood histamine level occur which may be divided into three distinct phases. First, a marked increase in the blood histamine which is present within an hour occurs in certain cases. Later, in all cases, a rapid and marked decrease takes place, the blood histamine content reaching its lowest level on the third to fifth day, the time at which edema and the signs of toxemia are most marked. There appears to be some correlation between the degree of damage and edema, and the decrease in the blood histamine, for such a decrease is most marked in the severe cases, and from Chart 4, it will be seen that in each instance where death occurred, the histamine content of the blood was well below the normal level 16 to 24 hours previously. As the edema subsides, the histamine level of the blood returns to normal or above. Such an increased blood histamine level may persist for some time. Of these three phases, that most consistently observed is the marked decrease in the histamine content of the blood as edema develops.

Previous investigations on blood histamine content in cases of burns by Barsoum and Gaddum,¹² and Code and MacDonald¹⁵ showed an increase in the blood histamine after the fourth or fifth day. The present investigations indicate that while an increase may occur at this time (as in Case 1 of our series) the blood histamine does not always rise above the normal. Barsoum and Gaddum¹² interpreted this rise as a possible cause of burn shock, whereas the present studies show that it occurs as the clinical condition of the patient is improving. It is probably for this reason that they had difficulty in attempting to correlate these changes with the onset of shock. Further examination of their results reveals that the blood histamine level was beginning to decrease in the cases that died. Although their diagrams do not indicate the actual day on which the determinations were made, a decrease in the blood histamine was apparently occurring in Case 1, and no determinations were made in Case 4 for at least four days before death. There was, however, a beginning decrease in the blood histamine level at this time. Thus, both in burns and in shock due to trauma or surgical intervention, a marked decrease in the histamine content of the blood occurs (Rose and Browne¹⁶). This is, therefore, contrary to the original conception that the histamine content of the blood must be increased during shock.

These results may perhaps be explained on the basis of previous work. In studies on allergic patients, one of us (Rose²⁰) has shown that stimulation of the skin of a patient with dermatographia may lead to rapid increase in the blood histamine which, in turn, is followed within 20 minutes by a decrease to below the original level as wheal formation takes place. Thus, as postulated by Lewis,²¹ irritation of the skin may result in a release of histamine. It has

been noted, further, that following the production of a large area of edema, such as is occasionally seen after the subcutaneous injection of a vaccine, or during the stage of swelling in angioneurotic edema, a marked reduction of the blood histamine usually occurs (Rose^{20, 22})

At this point, it may be well to note that in certain blood dyscrasias the total blood histamine may be increased as much as one hundred times without any symptoms being produced referable to the histamine (Code and MacDonald,¹⁵ Rose²³) This is due to the fact that under these circumstances the greatest portion of the blood histamine is held within the cellular elements (Code²⁴), and, as such, it is inactive. It is only when histamine is released from the cells of the blood into the plasma that it becomes active. On the other hand, a decrease in the blood histamine has been observed only during shock, or when marked edema of the skin and superficial tissues is present (Rose^{16, 20, 22}). Since a decrease in the blood histamine to below normal levels is usually correlated with such symptoms, it is felt that it may be of more clinical significance than an increase. This argument is supported, further, by the observation that following the subcutaneous injection of histamine, there is a decrease in the blood histamine as symptoms are produced (Rose²⁵), and this has also been noted following the intravenous administration of histamine (Rose²⁶).

In connection with the secondary increase of histamine in the blood, which is seen after the fourth or fifth day, it is interesting to note that an increase in the blood histamine has been observed in cases of chronic irritation of the skin (Rose²²).

Loos²⁷ has expressed the opinion that histamine may increase in the tissue about an area of inflammation, and this has actually been demonstrated in rabbits by Rocha E Silva and Bier,²⁸ and Tarras-Wahlberg.²⁹ Following the production of burns in dogs, Kisma³⁰ observed an initial increase in the histamine content of the blood followed in two to three days by a decrease. These changes were accompanied by an increase in the histamine content of the spleen, liver and pancreas. It may be that histamine is concerned with the shift of fluid from intra- to extracellular spaces and is, itself, transferred to the area of edema, whether it be the skin and superficial tissues, or the viscera.

The value of blood studies as a guide to the treatment of shock has been emphasized by Moon³¹ and Scudder.¹⁹ Although it is agreed that hemoconcentration is a criterion of shock, we have been struck by the number of instances where it was not present although, clinically, the patient was in shock, with a falling blood pressure and an increasing pulse rate. In all such cases, as, indeed, in others when hemoconcentration is manifest, the histamine content of the blood is always decreased to below normal. In the present studies, Case 3 illustrates a type of death which may have been influenced by the initial hemoconcentration. Yet, on the day of death, blood studies were normal with the exception of the blood histamine which was markedly decreased. In previous studies (Rose and Browne¹⁶ and Rose, Weill and

Browne³²) it has also been noted that patients may die in spite of the intravenous administration of amounts of plasma adequate to overcome hemoconcentration, as controlled by blood studies. The hemoglobin, hematocrit, plasma protein and other constituents of the blood, such as the chlorides, sodium and potassium may not be significantly altered under these conditions, but in all instances, there is marked diminution of the histamine content of the blood. As shown in the present cases, the administration of plasma may markedly reduce hemoconcentration without affecting the course of the blood histamine. A possible explanation is that the histamine remains low as long as the tendency to loss of fluid from the blood stream continues, even though by the use of intravenous fluids the blood volume may have been restored to normal so that no actual hemoconcentration exists at the time of taking the specimen. Thus, the blood histamine might be regarded as reflecting some process more fundamental than hemoconcentration in the causal chain of events leading to shock. From the present evidence, one cannot determine whether the changes in blood histamine are in any way causally related to the mechanism of hemoconcentration and shock. A reconsideration of its possible importance seems however to be justified since histamine shock, and shock due to trauma or burns may all be correlated with a decrease in the histamine content of the blood.

CONCLUSIONS

(1) Studies on the blood histamine, hemoglobin, hematocrit and plasma proteins have been made in seven patients following severe burns.

(2) It has been shown that a marked increase in the blood histamine occurs in certain cases within one hour after the burn. In all cases, there is a decrease in the blood histamine as toxemia and edema appear. As the edema and signs of toxemia disappear with the clinical improvement of the patient, the blood histamine rises to normal or higher levels. Such secondary increases in the blood histamine may persist above the normal for some time.

(3) There appears to be a definite correlation between the degree of damage and the decrease in the histamine content of the blood. Thus, the most marked decrease in the blood histamine has been noted 12 to 36 hours before death. Similar findings have been observed in other cases of fatal shock.

(4) Changes in the blood histamine do not appear to be altered by the administration of plasma in amounts sufficient to control hemoconcentration.

(5) These findings are discussed in relation to the changes observed in the histamine content of the blood in other conditions.

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A STUDY OF THE WEIGHT OF THE CELIAC GANGLION AND ITS RELATIONSHIP TO ESSENTIAL HYPERTENSION

REPORT UPON 201 CELIAC GANGLIA

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THE TREATMENT OF ESSENTIAL HYPERTENSION, which for so many years had been purely a medical problem, is now being taken up by surgeons all over the world. The surgical attack upon the problem of essential hypertension is quite varied. The exact surgical procedure employed is dependent upon the etiologic concept held by the surgical center where the patient happens to be. There are three surgical concepts of the etiology of essential hypertension, and as a result there are three methods of operative attack.

The first surgical concept considers essential hypertension as being due to hyperepinephrinemia. This theory is supported by De Courcy.⁸ The literature refuting this concept is voluminous.^{2, 9, 11, 15, 17, 18, 19}

The second surgical concept is the neurogenic theory held by Max Peet¹⁰ and the Mayo Clinic.¹ This concept, also, has been vigorously attacked by many recent workers, particularly by Goldblatt and his coworkers.^{12, 13, 14}

The third theory with surgical potentialities is that of Crile.⁴⁻⁷ This theory states that "only those individuals who have by inheritance large celiac and aortic ganglia can and do have hypertension."^{4, 5} Crile⁴ states that the average weight of the ganglion in cases of essential hypertension is 1,015 mg. for the left ganglion, and 669 mg. for the right ganglion. In the nonhypertensive group that he reported, the average weight of the celiac ganglion was found to be 310 mg. for the left ganglion, and 350 mg. for the right ganglion in cases of epilepsy. In recurrent hyperthyroidism, he found the average weight of the left celiac ganglion to be 235 mg., and the average weight of the right celiac ganglion to be 271 mg. In a group of cases with neurocirculatory asthenia, Crile reported the average left ganglionic weight as being 205 mg., and the right ganglionic weight 340 mg. In recent papers,^{6, 7} Crile states that the normal weight of the celiac ganglion in the nonhypertensive individual varies from 250 to 350 mg. The photographs shown by him also tend to show the markedly greater size of the celiac ganglion in cases of hypertension as compared with the celiac ganglion in nonhypertensive individuals.

The present study was undertaken for the purpose of determining the weight of the normal celiac ganglion and for the further purpose of testing the relationship of the size of the ganglion and essential hypertension. The literature does not contain such data as is presented here.

Anatomy of Celiac Ganglion—The anatomic descriptions given for the celiac ganglia differs with almost every author. The celiac ganglion has been described as being as large as a "nickel,"⁴ or a "strawberry."¹⁶ One anatomic

text describes it as being one inch in diameter.³ Many authors speak of its semilunar shape,²⁰ although most writers note variability in regard to this. Cline noted that the left celiac ganglion was usually larger than the right and he was the first to report the weight of the ganglia. All writers have uniformly agreed that the greater splanchnic nerve joins the celiac ganglion at the upper outer pole of the ganglionic mass.

In the series of cases which we studied (201 ganglia), we found a great variation in the size, shape, and weight of celiac ganglia. The left celiac ganglion was usually found to be larger than the right, the difference in size being very marked in some cases—in which the left ganglion was two to three times the size of the right. However, in many cases the weight of the right and left ganglia were almost equal. Occasionally, the right ganglion was found to be larger than the left. This difference in size has been unexplained as yet. It is possible that it may have to do with the close approximation of the left celiac ganglion to the aorta. A second possibility has to do with the possible relationship between the human "left handedness" and the larger left celiac ganglion. Functionally, however, since the area of nervous distribution is greater from the right than from the left celiac ganglion, one might expect the right ganglion to be the larger. Such was not usually found to be the case.

It was usually very difficult to separate the left ganglion from the adventitia of the aorta. Often, in the process of separation, the adventitia of the aorta was found attached to the under surface of the left ganglion. The right ganglion could easily be dissected free and the right aorticorenal ganglion could usually be differentiated from the celiac ganglion, whereas, on the left side, the aorticorenal ganglion was often fused with the left celiac ganglion to form a single fleshy mass.

Uniformly, the left celiac ganglion rested directly upon the aorta, whereas the right celiac ganglion rested upon the right crus of the diaphragm, under the inferior vena cava. In the vast majority of the ganglia that we dissected, the greater splanchnic nerve did not join the celiac ganglion at the upper outer pole of the ganglion, but rather joined it at its postero-inferolateral pole. We used this point of union with the greater splanchnic nerve to determine the lower limit of the celiac ganglion. The fleshy mass below this was considered as being aorticorenal. As stated, on the left side the aorticorenal ganglion is so intimately blended with the celiac ganglion that it was often impossible to separate them. Using our arbitrary lower limit of celiac ganglion as the point of junction of the greater splanchnic nerve with the ganglion, we cut the ganglionic mass flush with this point of union of the greater splanchnic nerve and the celiac ganglion. As a result, our specimens should represent celiac ganglion alone. For purposes of orientation on the specimens, the terminal half centimeter of greater splanchnic nerve was left attached to the celiac ganglion. On the right side, the aorticorenal ganglion was usually joined to the celiac ganglion by nerve fibers which were cut with ease. On this side, the lesser splanchnic nerve joins the lower ganglionic mass (aorticorenal ganglion) and the greater splanchnic nerve joins the upper ganglionic mass (celiac ganglion).

At times, both splanchnic nerves pierce the crus of the diaphragm at the same point, and travel together to the point of union of the greater with the celiac ganglion. Just before this union is made, the lesser splanchnic nerve may be seen coming off from the conjoined trunk and passing downward to the aorticorenal ganglion to unite with it. At times the greater and lesser splanchnic nerves do not travel together but pierce the crus of the diaphragm through separate openings. Invariably the greater splanchnic nerve pierces the diaphragmatic crus above the lesser splanchnic, the latter then comes out below and medial to the point of emergence of the greater splanchnic nerve. The same relationship of the two splanchnic nerves exists on the left side, but here the aorticorenal ganglion is so intimately blended to the celiac ganglion that the whole constitutes one large fleshy mass.

Usually the greater splanchnic nerves, after running along the vertebral column in a longitudinal course pierce the crura of the diaphragm on each side, and then suddenly make a right-angle turn medially and terminate in the celiac ganglion of the particular side at the postero-inferolateral angle of the ganglion. Often the greater splanchnic nerve passes behind the upper end of the celiac ganglion and gives one the impression that it is joining the upper end of the ganglion, but actually it passes downward behind the ganglion to join the ganglion at its lower outer pole, this anatomic feature provides a satisfactory boundary for determining the lower limit of the celiac ganglion. Sometimes the right-angle turn made by the greater splanchnic nerve forms a loop with a diameter of one centimeter. In almost all cases one can easily pick up the greater splanchnic nerve by passing the index finger downward along the bodies of the lumbar vertebrae and the crura of the diaphragm. When the palpating finger reaches the greater splanchnic nerve at its right-angle turn, the finger is halted by the loop formed by the angular turn of the nerve as it approaches the ganglion. Occasionally, the greater splanchnic nerve emerges from behind the crus of the diaphragm at a point one to two centimeters higher up than the celiac ganglion. In such cases, it passes downward in a straight course lying upon the crus of the diaphragm and then makes a right-angle turn medially and forward when it reaches the level of the celiac ganglion. The greater splanchnic nerve, in its abdominal course, varies from 0.2 to 0.4 cm. in thickness and is quite resistant to tearing.

There is an extreme degree of variation in the size of celiac ganglia. Some ganglia are one-half centimeter from side-to-side, and others measure two to three centimeters in the same dimension. The greatest diameter was generally from the lateral to the medial edge of the ganglionic mass, although in some of the triangular ganglionic masses the vertical measurements was the largest. There was also some degree of variation in thickness, but not to the same degree as in the other measurements. Some of the ganglia were about 0.2 cm. thick, while others measured almost 0.7 cm. in thickness. Figures 1-4 show some of the variations in size and shape found in celiac ganglia.

Variations in Ganglionic Weight with Sex, Age, and Size of Individual—There was an extreme degree of variation in weight of the ganglia which

ranged from small ones weighing 270 mg to very large ones weighing 2,000 mg. Among adults there was no correlation between the size of the individual and the size of the celiac ganglion. Some of the largest individuals had the smallest ganglia and *vice versa*. In three cases of pituitary dyscrasia in women who were found to weigh well over 300 pounds and to be over six feet tall, the celiac ganglia were found to be among the smallest in our collection.

FIG 1

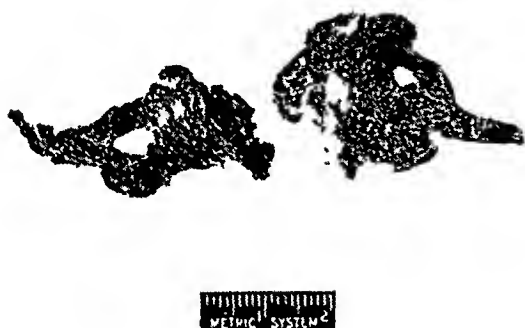


FIG 2



4

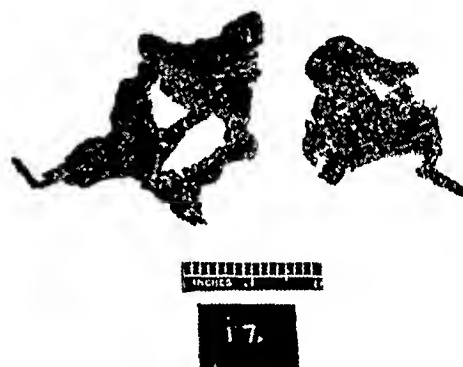
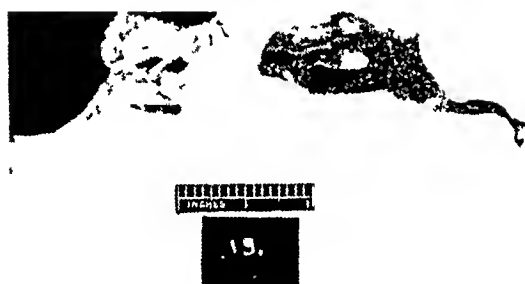


FIG 3

FIG 4

FIG 1—Left ganglion 1,466 mg	Right ganglion 1,082 mg	Patient I W, age 50 B P 138/84
Diagnosis Gangrene of leg		
FIG 2—Left ganglion 1,284 mg	Right ganglion 1,037 mg	Patient H L, age 67, B P 130/70
Diagnosis Pneumonia		
FIG 3—Left ganglion 1,330 mg	Right ganglion 1,113 mg	Patient A P age 50, B P 120/80
Diagnosis Pneumococcus meningitis		
FIG 4—Left ganglion 1,984 mg	Right ganglion 1,968 mg	Patient L G age 55, B P 120/80

Age appeared to be quite important in determining the size of the celiac ganglia. An examination of Charts 1 and 2 readily shows that there is an increase in weight of the celiac ganglia from birth to the 40- to 55-year-old group. After the age of 55, there tends to be a progressive decrease in the weight of the celiac ganglia. In the newborn, term infant, the average weight of the left celiac ganglion varies from 75 to 150 mg, and the right celiac ganglion weighs 50 mg. From infancy to the age of puberty, a progressive but not remarkable increase in the weight of the celiac ganglia can be noted (see tabulated case records). At the age of puberty, there appears to be a remarkable increase in the size of the celiac ganglia from the childhood to adult levels of weight. The ganglia in the 20- to 30-year-old group ranged from 400

to 900 mg. Only one ganglion in this age-group weighed as much as 1,400 mg. In the 30- to 40-year-old group, the general average of the weight of the ganglia was found to be about the same as in the previous age-group. The general average for this group was 814 mg. for the left ganglion, and 723 mg. for the right ganglion. The 40- to 50-year-old group had the largest-sized celiac

FIG 5

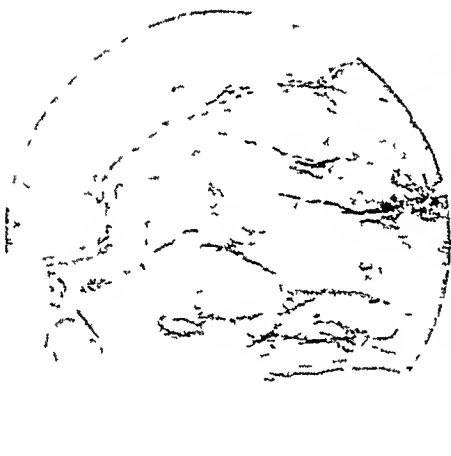


FIG 6

FIG 5—Photomicrograph of small celiac ganglion ($\times 20$). Note the small amount of extraneous tissue about the ganglion.

FIG 6—Photomicrograph of large celiac ganglion ($\times 15$). Note the small amount of extraneous tissue about the ganglion.

FIG 7—Photomicrograph of celiac ganglion showing characteristic histologic appearance of human celiac ganglion, i.e., groups of ganglion cells with dendritic fascicular tracts (high power).

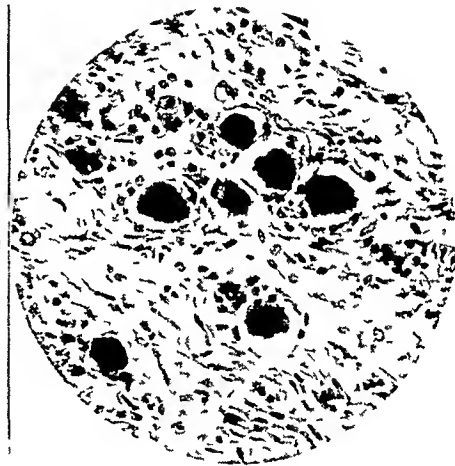


FIG 7

ganglia. In this group, the large-sized ganglia, not infrequently, weighed over 2,000 mg. It would seem that the celiac ganglia reach their maximum size during this decade. Following the 65-year-old group there appears to be a definite decline in the weight of the celiac ganglia. One of the smallest ganglia in our series was removed from a patient age 81.

The sex of the patient appears to account for a demonstrable weight difference. The average weight of the male celiac ganglion is greater than that of the female. The average weight of the left celiac ganglion in males was

found to be 1,140.5 mg, and the average weight of the left celiac ganglion in females was 779 mg. The average weight of the right celiac ganglion in the male was 894.3 mg, and that of the right celiac ganglion in females was 561 mg. The largest celiac ganglion in our series was found in a man. It weighed 2,100 mg. The largest celiac ganglion removed from a woman weighed 1,461 mg.

Relationship between the Weight of the Celiac Ganglia and Essential Hypertension—One of the foremost exponents of the surgical treatment of essen-

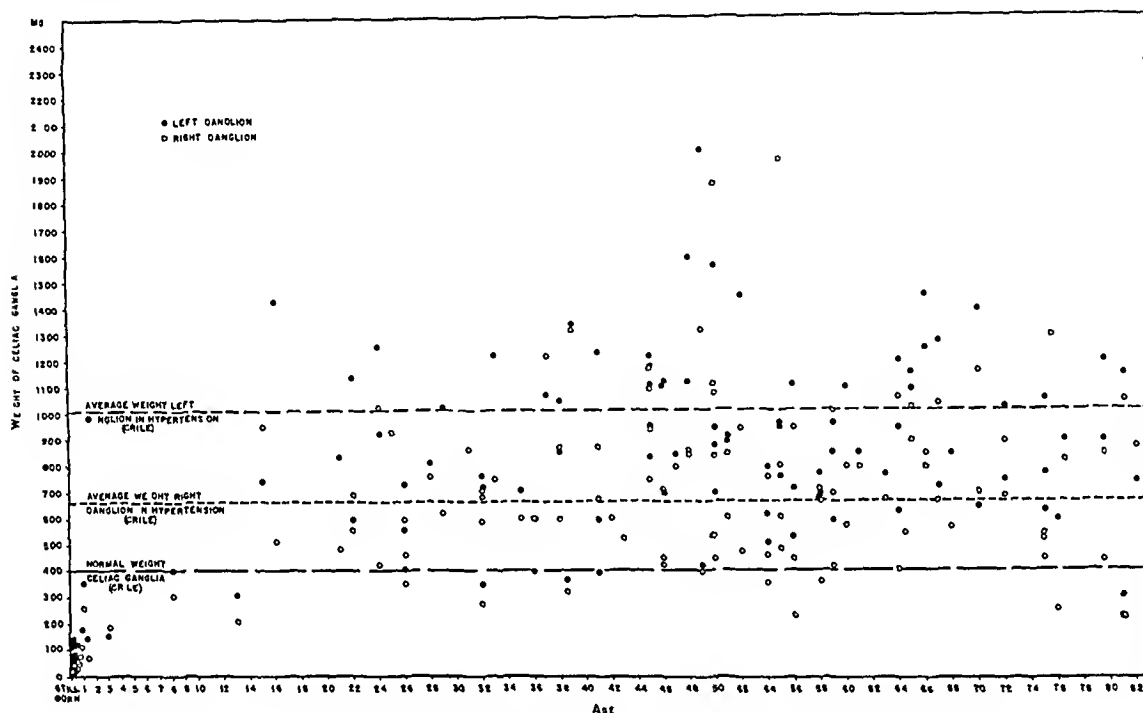


CHART 1—Diagnosis Pneumonia Scattergram plotting the weight of the celiac ganglia against the age of the patient

tial hypertension (Crile) bases his etiologic concept upon the premise that, "the celiac ganglion is larger in the individual with essential hypertension than in the nonhypertensive." He quotes the weight of the left ganglion as being 1,015 mg. in hypertensive individuals, and that of the right as being 669 mg., whereas the average normal ganglionic weight was only 350 mg. If it is true that the celiac ganglia are larger in individuals with essential hypertension than they are in nonhypertensives, then the operation of celiac ganglionectomy, based upon the above premise, is justifiable. If it is not true then the whole hypothesis has no basis since its premise is false.

Method—With the idea of substantiating Crile's statements as to the weight of the celiac ganglion, we collected a large number of celiac ganglia. Our ganglia were all removed from autopsy material as soon after death as possible. The celiac ganglia were identified by following the greater splanchnic nerve at its point of emergence from behind the crus of the diaphragm. The terminal centimeter of the greater splanchnic nerve was removed with the celiac ganglion for purposes of identification, as can be readily noted in Figures 1-4. The ganglia were cut flush with the point of attachment of the greater splanchnic nerve, as we considered everything below

this point to be aorticorenal ganglion. After the removal of the ganglia, they were thoroughly dissected free of all extraneous material, and were then weighed on a fine balance inclosed in a glass case, and the weighing was carried to the milligram. Several ganglia were serially sectioned and microscopically examined to note the amount of extraneous tissue present. Figures 5 and 6 show the very small amount of extraneous tissue present after the dissection. After the ganglia had been removed, some of the earlier ones had been put into a bottle of 10 per cent formalin and suitably labelled as to right

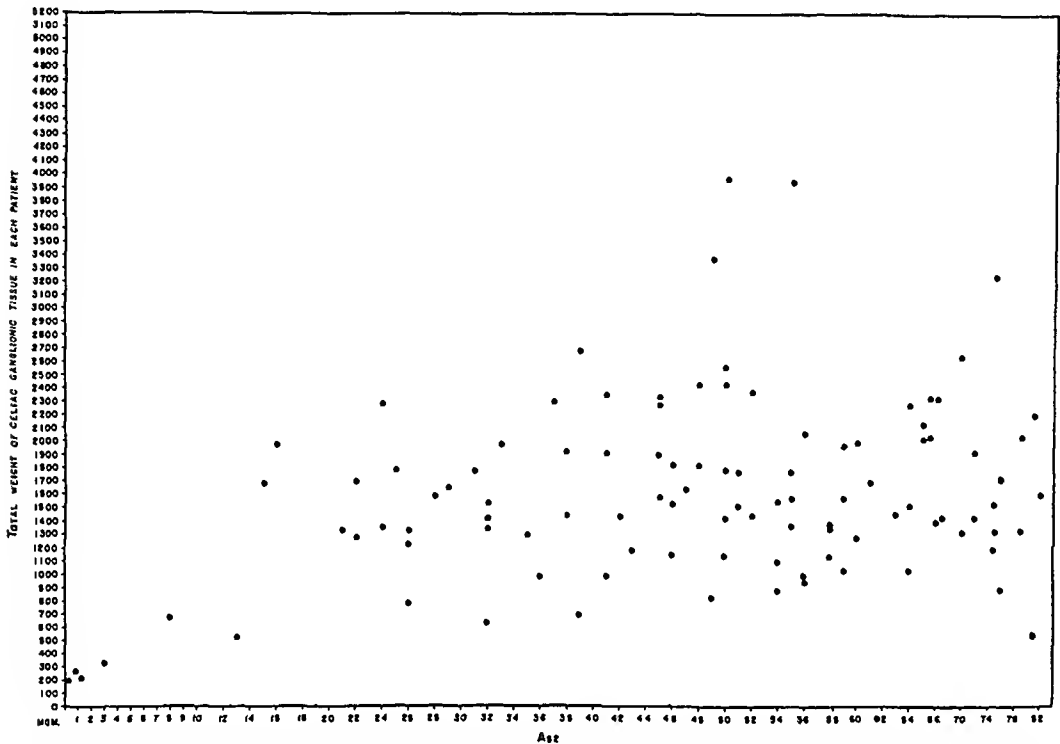


CHART 2.—Scattergram plotting the total ganglionic weight obtained by adding the weights of the left and right celiac ganglia against the age of the patient. The total ganglionic weight reported in his hypertensive group was 1,682 mg. (Crile)

or left side. These ganglia were not dissected clean or weighed for five weeks. In order to determine whether the fixation in formalin would add materially to the ganglionic weight, three of the ganglia were weighed in the fresh state immediately after removal and dissection, and were then weighed at varying intervals of time subsequently. By so doing, we found that the celiac ganglia increased in weight for the first week. During this period of time between 15–20 mg of weight was added to the original weight of the fresh ganglion. After the first week, however, there was a progressive loss of weight, such that by the end of the fifth week the celiac ganglia weighed from 25–40 mg less than they did in the fresh state.

It is thus apparent that the celiac ganglia do not gain weight when immersed in formalin after the first week. Since the ganglia in our series were either weighed immediately after the autopsy or five weeks later, it is apparent that we are being conservative in determining the true celiac ganglionic weight since we did not add the known loss of weight to the resulting weight obtained

at the end of five weeks' fixation. The celiac ganglionic weights obtained in our series of ganglia were all uniformly higher than those obtained at the Cleveland Clinic. The small tag of greater splanchnic nerve which we permitted to remain attached to the celiac ganglia does not add materially to the final result, and, certainly, does not account for the wide difference between our results and those of the Cleveland Clinic.

Results—An attempt was then made to correlate the size of the celiac ganglia with the blood pressure of the patient in order to determine whether

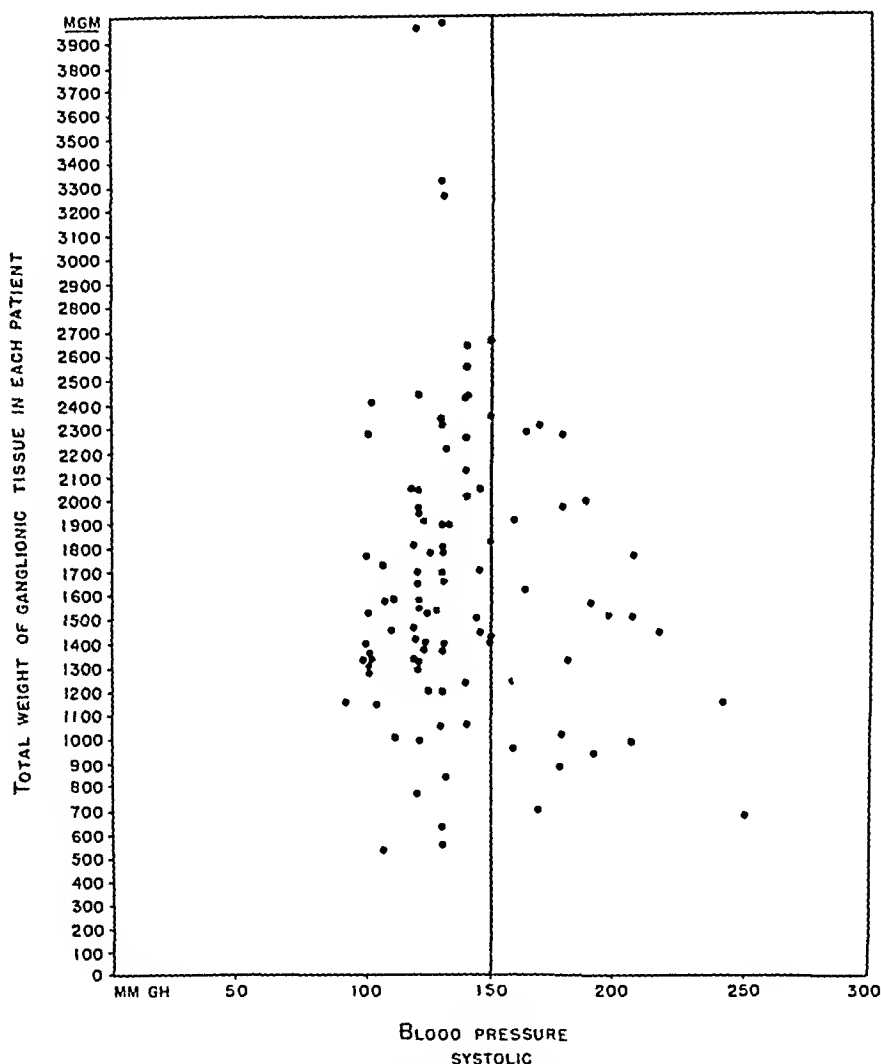


CHART 3—Scattergram plotting the total ganglionic weight against the systolic blood pressure. Note that the total ganglionic weight reported in Crile's hypertensive group was 1,682 mg.

there was really an increase in size of the celiac ganglia in hypertensive individuals. An examination of Charts 1, 2, and 3 furnishes adequate evidence that the vast majority of the large ganglia weighing in the neighborhood of 1,000 mg, or more, were well within the normal blood pressure range, and that in the hypertensive group the celiac ganglionic weights were actually somewhat less than in the nonhypertensive group. The largest ganglion collected weighed 2,100 mg, and was found in a nonhypertensive individual, whereas the largest ganglion found in an hypertensive individual weighed 1,250 mg. Both these ganglia were on the left side. The right celiac ganglion

that was the largest in the nonhypertensive group weighed 1,950 mg, while the heaviest right celiac ganglion in the hypertensive group weighed 1,225 mg. On Figure 5 a cross-line, indicating the level which the Cleveland Clinic considers to be the normal celiac ganglionic weight in the nonhypertensive group (350 to 400 mg), is seen to be far below the average weight of the celiac ganglia in our nonhypertensive group. Practically all of the celiac ganglionic weights in the nonhypertensive group in our series of 200 ganglia fall well within the range of ganglionic weights quoted by Crile as character-

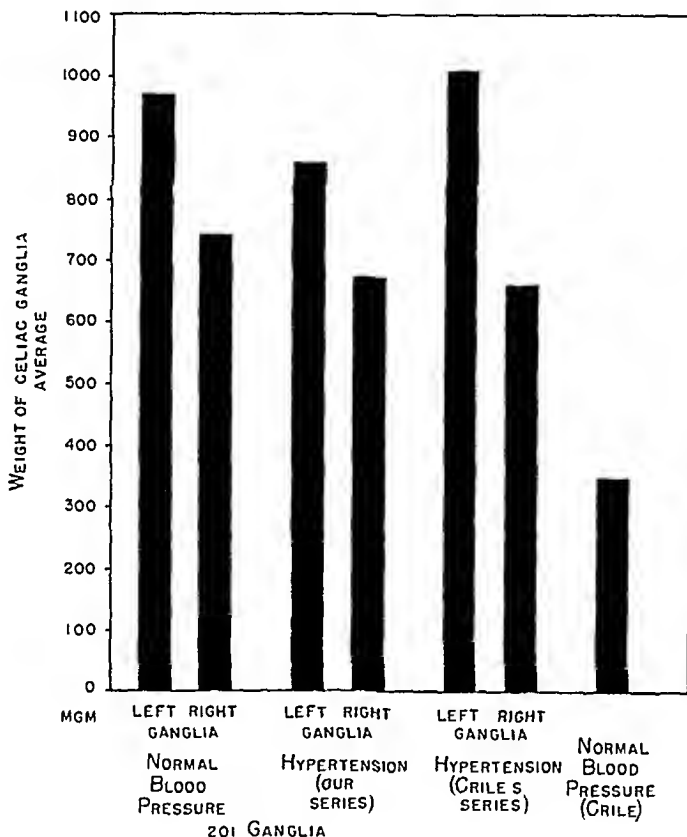


CHART 4—Graphic presentation of the average weight of the left and the right celiac ganglia in our series of hypertensive and nonhypertensive individuals as compared with Crile's results for the same groups

izing the hypertensive group. Chart 4 is a graphic representation of the average weight of the left and right celiac ganglia in our series of cases in the nonhypertensive group and in the hypertensive group, in comparison with the statistics quoted by Crile for the same two groups in his series. A survey of this shows that the average weight of the left celiac ganglion in our nonhypertensive group was 968.4 mg, and the average weight of the right celiac ganglion in our nonhypertensive group was 745 mg. The average weight of the left celiac ganglion in our hypertensive group was seen to be 867.9 mg, and the average weight of the right celiac ganglion in the hypertensive group was found to be 674.4 mg.

These results, when considered in the light of the difference in the numbers of cases in each group, reveals a startling uniformity of result. It becomes

quite obvious that the hypertensive group do not have larger celiac ganglia than the average normal nonhypertensive in the same age-group, and also that the average normal ganglionic weight is far greater than that quoted by Crile. The amazing equality of ganglionic weights in our group of normal individuals, and in Crile's group of hypertensive individuals can mean only one thing—that is, that there is no difference in the celiac ganglionic weight in the non-hypertensive and in the hypertensive individual, and that our equality in the average weights obtained in both groups merely represents the mean average of the celiac ganglionic weights on the left and right side in all individuals, irrespective of the presence or absence of hypertension.

SUMMARY AND CONCLUSIONS

(1) The greater splanchnic nerve unites with the celiac ganglion at the postero-infero-external angle (of the ganglion) and not at the upper pole as formerly stated.

(2) The celiac ganglia vary greatly in size and shape. No two ganglia have exactly the same shape. The point of union of the greater splanchnic nerve with the lower pole of the celiac ganglion, we considered as being the lower limits of the celiac ganglion proper, everything below this point, we called the aorticorenal ganglion.

(3) The celiac ganglia increase in size from birth until the age of 40 to 55 years. In this age-group, the celiac ganglion appears to attain its maximum size and weight. After this is a gradual decline of the ganglionic weight to a level that, in the octogenarians, is near the childhood level.

(4) The left celiac ganglion is uniformly larger than the right.

(5) There is a definite difference in the sizes of the celiac ganglia in the two sexes. The largest ganglia were found in the male sex.

(6) There is no correlation between the weight of the celiac ganglion and essential hypertension. The average weight of the celiac ganglion in the hypertensive group was somewhat less than the average weight of the ganglia in the nonhypertensive group. This was undoubtedly due to the difference in the number of cases in each group.

(7) Our average weight of the left celiac ganglion in the nonhypertensive group was 969 mg. This coincides closely with the average weight of the left celiac ganglia removed by Crile surgically from hypertensives (1,015 mg.)

(8) The average weight of our right celiac ganglia in the nonhypertensive group was 745 mg. This was somewhat higher than the weight of the right celiac ganglion reported by Crile for his hypertensive group (667 mg.)

(9) The total ganglionic weight in Crile's hypertensive group was 1,682 mg, whereas the total ganglionic weight in our nonhypertensive group was 1,714 mg. The total ganglionic weight represents the sum of the weights of the left and the right celiac ganglia in each individual.

(10) From the preceding data, we feel that new standards of weight for the celiac ganglia should be established, and that there is no relationship between the weight of the celiac ganglion and essential hypertension.

TABLE I

SUMMARY OF DATA RELEVANT TO CELIAC GANGLIA EXAMINED IN 101 CADAVERS

	Name	Age in Years	Left in Mg	Right in Mg	Sex	Blood Pressure	Diagnosis
1	B M	8	400	281	M	250/158	Polycystic kidneys
2	M H	13	313	207	F	115/75	Diabetic coma
3	J L	15	745	943	F	144/80	Rheumatic pancarditis
4	L G	16	1 461	514	F	120/80	Miliary tuberculosis
5	E O	21	834	485	F	120/80	Tuberculous peritonitis
6	J C	22	581	691	F	100/60	Bacterial endocarditis
7	S S	22	1 135	564	M	120/80	Peritonitis
8	M H	24	928	428	F	126/78	Intestinal obstruction
9	W K	24	1,252	1,021	M	180/120	Chronic nephritis with uremia
10	W C	25	865	929	M	132/88	Tuberculous meningitis
11	W F	26	730	600	F	100/70	Peritonitis
12	J F	29	1 026	628	F	130/80	Postpartum hemorrhage
13	M L	26	405	358	F	120/80	Acute pancreatitis
14	H P	31	913	864	F	128/80	Puerperal sepsis
15	G L	28	816	767	F	110/70	Septicemia
16	J R	26	568	465	F	140/95	Degeneration of liver
17	R R	32	722	682	M	120/80	Mesenteric thrombosis
18	W D	32	832	704	M	100/60	Lung abscess
19	E G	32	765	594	F	102/60	Peritonitis
20	M R	32	353	270	F	130/80	Pneumonia
21	S R	33	1 226	748	F	120/75	Subphrenic abscess
22	P L	35	702	596	F	101/78	Carcinoma of breast
23	E F	36	395	590	F	120/80	Lobar pneumonia
24	L L	37	1 073	1 224	M	165/110	Intestinal obstruction
25	S M	38	852	605	F	110/70	Angiosarcoma
26	L D	38	1 047	871	M	128/80	Brain abscess
27	F J	39	1 340	1 333	M	150/90	Brain tumor
28	F L	39	371	325	F	170/130	Brain tumor
29	G D	41	1,236	675	F	134/80	Peritonitis
30	N Q	41	600	392	F	110/60	Bacterial endocarditis
31	T B	41	1,471	882	M	150/70	C N S syphilis
32	I E	42	837	605	F	220/100	Chronic nephritis with uremia
33	H B	45	955	945	M	130/80	Bacterial endocarditis
34	S S	43	653	532	F	125/80	Carcinoma uterus
35	C P	45	826	747	M	120/80	Myocarditis
36	M B	45	1,216	1 101	M	170/90	Cerebral hemorrhage
37	Z I	45	1 102	1,170	M	100/68	Pneumonia
38	A K	46	1,120	420	M	129/86	Perinephritic abscess
39	M D	46	1,112	701	F	150/70	Acute thyroid crisis
40	A F	46	700	450	F	90/65	Bacterial endocarditis
41	W S	47	857	792	M	120/80	Cirrhosis of liver
42	O G	48	1,594	836	M	140/70	Pyonephritis
43	P M	49	2 005	1 316	M	130/80	Peritonitis
44	P C	49	432	405	F	134/82	Carcinoma of cervix
45	C W	50	696	457	M	240/130	Nephrosclerosis with uremia
46	F F	50	2,100	1,870	M	130/80	Pneumonia
47	J P	48	1,121	680	M	120/80	Bacterial endocarditis
48	L L	50	1 570	—	M	125/80	Pneumonia
49	M B	50	956	844	M	130/80	Leukemia
50	L W	50	1,466	1,082	M	138/84	Gangrene of leg
51	A P	50	1,330	1,113	F	120/80	Pneumococcus meningitis
52	E E	51	894	613	M	200/120	Pontine hemorrhage
53	A B	51	906	860	M	100/60	Lung abscess
54	T B	52	1,441	944	F	104/88	Cardiac failure rheumatic heart disease
55	R L	52	973	475	M	145/90	Leukemia
56	H M	50	887	534	F	150/84	Carcinoma of cervix
57	B R	54	514	362	F	180/100	Carcinoma of liver
58	G W	54	622	470	F	130/80	Acute pancreatitis
59	E H	54	790	765	F	120/84	Carcinoma of sigmoid
60	L G	55	1,984	1 968	M	120/80	Lobar pneumonia
61	E Z	55	965	612	F	110/70	Lobar pneumonia
62	M G	55	961	808	F	210/100	Ovarian hemorrhage

CELIAC GANGLION AND HYPERTENSION

TABLE I (Continued)

	Name	Age in Years	Left in Mg	Right in Mg	Sex	Blood Pressure	Diagnosis
63	E C	55	768	590	M	128/80	Bronehogenic carcinoma
64	G H	56	715	235	F	160/110	Pulmonary embolus
65	R S	56	1,115	941	F	122/78	Pneumonia
66	C A	58	763	380	F	105/70	Myelogenous leukemia
67	L K	56	531	432	F	210/115	Cerebral hemorrhage
68	E P	58	687	693	F	120/80	Pneumonia
69	H C	58	706	678	F	125/80	Postoperative peritonitis
70	P H	59	963	1,005	M	180/120	Coronary occlusion
71	L B	59	868	701	F	190/110	Peritonitis
72	A M	59	596	435	F	180/140	Nephrosclerosis, with uremia
73	M V	60	713	576	F	120/70	Carcinoma of stomach
74	H C	60	1,135	865	M	190/120	Coronary occlusion
75	A Y	61	865	532	M	130/80	Lobar pneumonia
76	F G	63	777	677	M	118/84	Tuberculous kidney
77	G P	64	1,200	1,065	M	140/88	Carcinoma of bladder
78	D G	64	950	560	F	125/75	Carcinoma of ovary
79	M Z	64	633	105	M	140/90	Cerebral hemorrhage
80	A H	65	1,090	917	M	140/80	Cardiac failure, aortic stenosis
81	A A	65	1,124	1,005	M	140/90	Chronic nephritis
82	S S	66	1,245	706	F	148/82	Myocardial failure, arteriosclerotic heart disease
83	J B	66	1,167	554	M	130/90	Aortic stenosis
84	H I	67	1,281	1,037	M	130/70	Pneumonia
85	A P	67	724	672	F	104/60	Carcinoma of pancreas
86	S L	68	856	569	M	145/86	Pyonephritis
87	A S	70	638	679	M	120/70	Lobar pneumonia
88	J C	70	1,485	1,161	M	140/80	Carcinoma of prostate
89	L C	72	745	651	F	150/80	Cardiac failure, arteriosclerotic heart disease
90	J T	72	1,028	897	M	160/104	Coronary occlusion
91	K S	75	635	558	F	130/84	Pneumonia
92	R F	75	1,052	153	F	210/120	Cardiac failure, essential hypertension
93	A F	75	783	527	F	180/100	Carcinomatosis
94	M F	75	1,921	1,324	M	130/80	Coronary occlusion
95	A P	76	663	267	F	192/110	Cardiac failure, essential hypertension
96	M S	76	897	828	M	110/70	Carcinoma of liver
97	J R	79	1,195	851	M	118/80	Carcinoma of pancreas
98	H H	79	894	445	M	100/60	Abseess of kidney
99	S W	81	317	234	F	130/80	Ovarian hemorrhage
100	R B	81	1,152	1,052	M	136-78	Cystic liver
101	L T	82	763	876	M	165/90	Cardiac failure, arteriosclerotic heart disease

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MALIGNANT TUMORS OF SYNOVIAL ORIGIN

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DURING the last decade, and particularly the last three years, a small group of investigators has endeavored to add to our very limited knowledge of malignant tumors which take their origin from the synovial-lined structures, namely, joints, bursae and tendon sheaths. This field has too long remained neglected by pathologists. Owing both to the relative infrequency of these tumors and, what is more likely, the failure to classify them properly, the number of cases reported has been small. It has been difficult, therefore, to draw any conclusions as to the most satisfactory method of treating them. This report is based on the cases on file at the Army Medical Museum upon which the diagnosis of synovioma has been made. Its purposes are to increase the present small number of previously reported synoviomata, to point out the microscopic pathology characteristic of the majority of these cases, and to suggest a plan of treatment which, in the light of our limited knowledge, seems both rational and conservative. Where the material has been received from physicians in civilian practice, it has been impossible in some instances to obtain an adequate description of the gross pathology as well as a complete history and follow-up.

This study treats only with those tumors arising from the joint capsule, bursal wall or tendon sheath which are malignant, or border-line, and does not include the more common giant cell tumor or xanthoma which may arise from either of the three structures. The term synovioma was first coined by Lawrence Smith¹ to designate those tumors arising from all three synovial-lined structures. This marked a departure from the old method of classifying these new growths separately. The earlier reports were further clouded by the confusion surrounding the actual origin of synovial tissue. For a long time it was held to be endothelial in character and, on this basis, tumors arising from these structures were designated as endothelial sarcoma, angiosarcoma, and endothelioma. The synovial membrane is now generally accepted as mesenchymal in origin. It may be divided into two parts histologically—the outer wall, which is composed of dense connective tissue known as the fibrous layer, and the inner or synovial layer, which is more cellular and thought by many to secrete the viscid colorless liquid of the joint cavity. The transition between the two layers is not well delineated and most investigators believe that these more cuboidal cells of the inner lining are only a more highly differentiated form of the connective tissue cells forming the outer layer. This inner layer is not infrequently thrown into pronounced folds which may be temporary formations depending upon the position of the joint, or they may form permanent villi which project into the cavity. Special emphasis is made at this point of the not uncommon tendency to villous formation. Later it will be shown that the majority of cases in

this series present a pathologic pattern which might well be described as a distorted attempt at villi formation

As early as 1910, Lejars and Rubens-Duval² made the first real contribution to the classification of these tumors. According to these writers, there may be two types of malignant tumors arising from these structures depending upon what part of the capsule or tendon sheath the tumor takes its origin. If the cells develop from the fibrous layer, one cannot distinguish the tumor microscopically from the common fibrosarcoma, but if it arises from the inner layer whose cells, as noted previously, are more epithelioid in character, the pattern may strongly suggest synovial tissue as the origin of the tumor. It behooves the surgeon, therefore, to make careful note of the anatomic relationship of the tumor at the time of operation, as this may be of material aid in differentiating between the fibrous type of synovial tumor and the more common fibrosarcoma. It is probably because of this failure that all of the cases of this series belong to the second or synovial group, and undoubtedly those arising from the fibrous layer were simply classified as fibrosarcoma.

In making the diagnosis in the nine cases comprising this series, the history, clinical features and pathologic appearance have all been taken into consideration. In practically every incidence there has been uniformity of opinion among the pathologists to whom sections were submitted, otherwise the case was not included.

Incidence—The study of previously reported cases of synovioma discloses a tendency for this type of tumor to occur between the third and fifth decades. With one exception, this was borne out in this series. The age of two cases was 17, and the remaining seven were between 21 and 42. Four were male, and five were female. All of the patients in this series were white.

Duration of Symptoms—In this entire group of cases, swelling was the initial symptom. The time interval from the discovery of the swelling until medical consultation varied from three months to six years, the average being approximately two years. This, in itself, would indicate that pain was not an outstanding feature.

Pain—Five of the nine cases complained of pain at the time of their first examination. In only one, however, was it described as severe.

Trauma—A history of previous injury to the affected part was obtained from three patients, but in each it was relatively mild. The earliest development of a tumor following injury was three months.

Tumor—The size of the swelling on examination varied between that of an olive and a hen's egg. It is interesting to note that in five cases the character of the tumor was described as cystic.

Location—The tumors occurred most frequently in a lower extremity. Five developed about the knee, two arose from the region of the external malleolus, and one was located on the plantar surface of the foot. The remaining case originated on the right forearm near the elbow.

Roentgenographic Examination—Roentgenographic studies revealed the shadow of a soft tissue tumor, but no bone involvement in any of the cases.

Operative Findings—Unfortunately, in the majority of the cases the descriptions of the operative findings were very meager. Of the nine cases, three were reported as being encapsulated grossly. In three instances, the attachment to tendon sheaths was noted. The tumor, in one case, completely filled the suprapatellar and popliteal bursae and invaded the joint cavity at two points. Although the microscopic sections in a majority of the cases would indicate the rather vascular nature of the tumors, no observations were made at operation which would bear this out. Two cases were of particular interest in that the tumor removed at first operation was reported as a benign cyst.

Gross Pathology—The gross examination of the specimens revealed one uniform finding—in all there was a tendency to cyst formation. In some, however, it was very pronounced, whereas in others this feature was less marked. The cysts contained either straw-colored or bloody fluid and one might suspect that the tumor cells continue the highly specialized secretory function of the parent synovial cell.

In general, the tumor was described as being poorly encapsulated, although as previously noted there was a definite capsule in three cases. The tumor itself was usually lobulated and soft in consistency. In one instance where the tumor was quite large, there were gross areas of necrosis. Their color varied from a grey to a faint yellow. In the one case where a metastatic inguinal node was removed for study, its gross appearance conformed to that of the original tumor.

Microscopic Pathology—The striking similarity in the histologic pattern of the majority of the cases herein reported should demand special emphasis. Since 1910, when Lejars and Rubens-Duval first classified malignant joint tumors, observers have noted, from time to time, the peculiar epithelioid-like cuboidal cell which is so characteristic of these tumors. They have pointed out their probable relationship to the mesothelial lining cells of the joint cavities, bursae and tendon sheaths. Here, however, their analogy has stopped. This investigator was struck by the tendency of these tumors to form a papillary pattern which is not unlike the papillary projections found in villous arthritis. It is hardly possible that there is any etiologic association, yet, in synovioma we seem to have an attempt to form villi. In six of the nine cases of this group this pattern is found throughout the entire tumor, while in the others, although present, it is only seen in part of the section. Frequently the small cysts noted in the gross reveal, on microscopic examination, papillary buds projecting into the cyst lumina. The central portion of the papillary projections is composed of a stroma of fairly typical fibroblasts. Blood vessels are numerous. This central framework is covered by a layer of cells of a more cuboidal type with large vesicular nucleus and acidophilic cytoplasm. The thickness of this layer may vary from one to three cells, but there is no sharp line of demarcation between these larger cells and the more fibroblastic cells which form the stroma. In the spaces between the projections, there may be clear pink-staining fluid, and often hemorrhage is present. Where the

cells are more densely packed and the papillary formation is absent, the two types of cells described above may be found lying in adjacent bands. Mitotic figures are present but not numerous.

CASE REPORTS

Case 1—Acc 46896 E. D., a white, female, age 17, with synovioma in the region of the external malleolus of the right ankle.

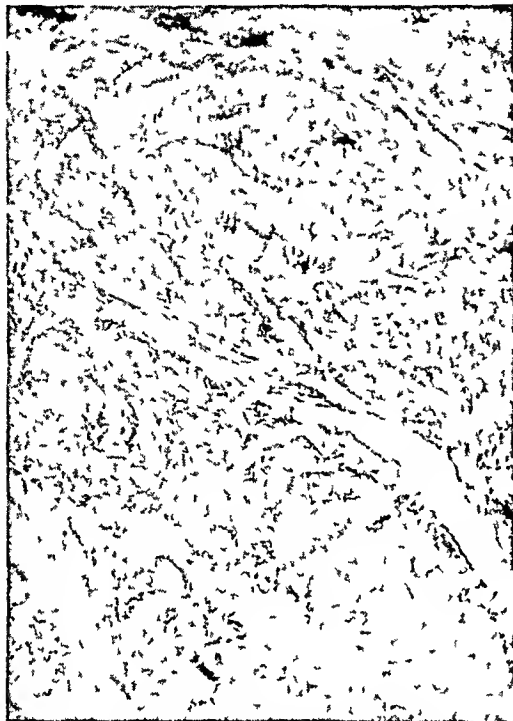


FIG 1—Case 2 Synovioma showing papillary arrangement of cells ($\times 100$)

section showed a pale grey homogeneous surface with small cystic areas containing blood. *Microscopic*—A richly cellular tumor which for the most part is composed of closely packed polyhedral cells with large vesicular nuclei. Mitotic figures are common. There are several areas of hemorrhage and necrosis. Numerous small cysts are present which are lined by cuboidal cells and show papillary projections.

Subsequent History—Patient received extensive roentgenotherapy to right ankle and inguinal regions. In 1936, examination disclosed an ulcer at the site of the original lesion. Two years later she developed evidence of pulmonary metastases, and died April, 1938. No autopsy was obtained.

Case 2—Acc 37019 E. A., a white, female, age 45, with synovioma in the region of the attachment of the biceps femoris tendon.

History—Four years prior to her admission to the hospital, the patient first became aware of a swelling on the lateral surface of her left leg just below her knee. There was no history of previous trauma. The growth slowly increased in size until it was as large as a hen's egg. It was moderately painful to pressure.

Examination—A smooth, soft tumor, 6x4x4 cm, was found on the lateral surface of the leg about the level of the head of the fibula. The tumor seemed attached to the deep structures, but the skin over it was freely movable. There was no swelling of the joint. Some tenderness could be elicited on moderate pressure over the tumor. Roentgenograms showed no evidence of bone involvement.

History—In 1933, four months before admission to the hospital, the patient received a mild blow on the external surface of her right ankle. No significance was attributed to the injury until a small lump developed at this site. It was described as soft and cystic, approximating the size of an olive. Following excision by her physician, the wound failed to heal until the patient was given roentgenotherapy four months later. In 1934, there was a local recurrence of the tumor. A biopsy, made at this time, was reported as an angiosarcoma. Under further roentgenotherapy, the tumor again disappeared only to return again a year later.

Examination—At the site of the operation there were several small pea-size nodules which were soft in consistency. These appeared to be adherent to the skin. There was no swelling of the joint itself. In the right inguinal region, there was an enlarged lymph node the size of a hen's egg.

Operation—Excision of inguinal node.

Pathologic Report—*Macroscopic*—A

soft oval tumor about 4.3x2 cm, which on

Operation—March, 1932, a tumor, which seemed to arise from the biceps femoris tendon, was excised

Pathologic Report—*Macroscopic* A well encapsulated, firm tumor which on section appeared to be lobulated. There were no cystic areas present. The cut surface was a dull grey with occasional areas of hemorrhage. *Microscopic* A rather vascular tumor which displays mainly two types of cells with a marked tendency to papillary formation (Fig 1). The fibroblastic or spindle-shaped cell seems to form a basement membrane for these projections, and the more cuboidal type of cell comprises the outer layer which



FIG 2—Case 2. The basement membrane of fibroblasts covered by the more typical cuboidal cell ($\times 400$)

varies from one to four cells in thickness (Fig 2). These cells show a vesicular nucleus. Some of the spaces between the papillary projections are filled with hemorrhage.

Subsequent History—Following operation, the patient received intensive roentgenotherapy at the Walter Reed Hospital. In June, 1939, seven years after discharge from the hospital, the patient reports that she is well and has had no evidence of a local recurrence of the tumor.

Case 3—Acc 39605 M D, a white, female, age 30, with synovioma developing on the plantar surface of the left foot.

History—In 1930, the patient had what was thought to be a simple benign cyst excised from the plantar surface of the left foot. The duration of symptoms prior to this operation was not given, but two and one-half years after it a swelling developed at the

site of operation and slowly increased in size causing local pain and discomfort on walking

Examination—On the plantar surface of the left foot lying beneath the scar of a previous operation, there was a flattened, lobulated tumor just proximal and lateral to the base of the great toe. It was not attached to bone or to the overlying skin. Roentgenologic examination was negative.

Operation—March 3, 1933, a lobulated nonencapsulated tumor, 3x1.5x1.5 cm, was excised from the region of the base of the great toe. It lay beneath the plantar fascia.

Pathologic Report—*Macroscopic* No description given. *Microscopic* The picture presented here is identical to that of Case 2. Characteristically, the epithelioid type of cell is found overlying those more spindle in appearance. The papillary structure is equally pronounced. (Figs 3 and 4)



FIG 3—Case 3 Synovium with the typical papillomatous pattern ($\times 100$)



FIG 4—Case 3 High magnification to show villous like structure so characteristic of the entire tumor ($\times 500$)

Subsequent History—Following operation, the patient received a course of roentgenotherapy, but in 1935, two years later, the tumor recurred and grew rapidly. At reoperation it was found to involve most of the tendon sheaths on the plantar surface of the foot. Further roentgenotherapy was given, with only temporary benefit, and, in 1937, the foot was amputated because of extensive ulceration of the plantar surface. Two months later she developed an inguinal mass. Her course from this point was steadily downhill, with death from pulmonary metastases in December, 1938.

Case 4—Acc 60073 V S, white, female, age 22, with synovium developing in the region of the left ankle.

History—Two and one-half years before admission to the hospital, the patient fell, striking her left ankle. A slight swelling, which was not particularly painful at first, developed several months later and at the end of two years it had increased noticeably in size.

SYNOVIOMA

Examination—Below the internal malleolus of the left ankle, and extending on to the plantar surface of the foot along the longitudinal arch, there is a soft cystic swelling. The area over the tumor was exquisitely tender. Roentgenograms were negative for any bone involvement.

Operation—On October 10, 1938, a tumor was excised which extended from the os calcis to the heads of the metatarsals beneath the plantar fascia. It was described by the operator as being well encapsulated and extremely vascular. There was no contact with any bony structure.

Pathologic Report—Macroscopic A granular, greyish mass with occasional yellow spots, but no definite cystic areas. As the tumor had not been removed in one piece,

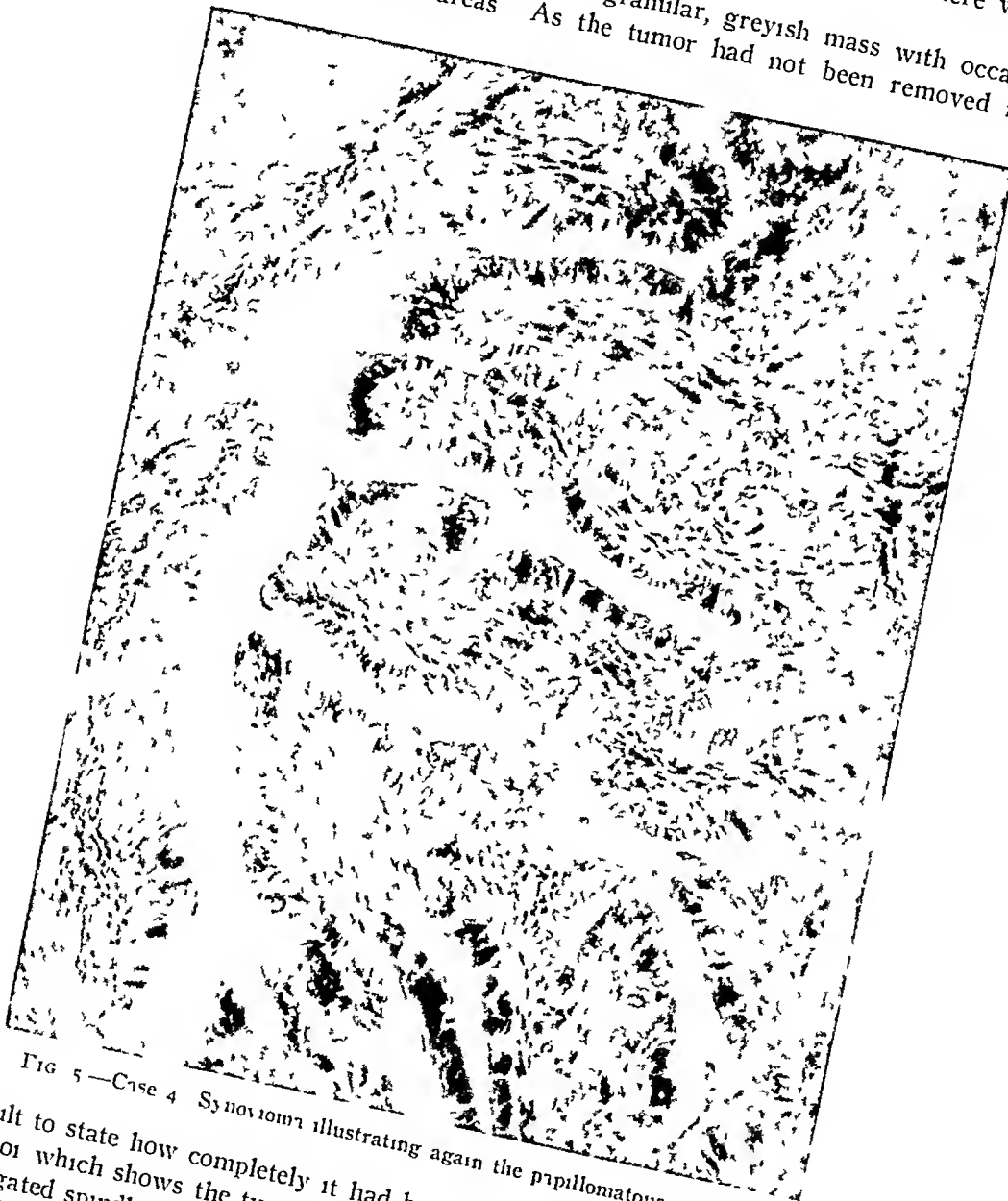


FIG 5—Case 4. Synoviomia illustrating again the papillomatous structure.

it was difficult to state how completely it had been encapsulated. *Microscopic* A highly vascular tumor which shows the typical papillary pattern. These papillae have a framework of elongated spindle cells and are covered by cells which closely resemble columnar epithelium (Fig 5). In some fields the line of demarcation between these two types of cells is striking, but more commonly the epithelioid cells fade into the spindle-shaped cells without any sharp line of division. Mitotic figures are not prominent in this tumor.

Subsequent History—Following operation, the patient received radiation therapy. On examination, 18 months later, she appeared in an excellent state of health, with no evidence of local recurrence of the tumor.

Case 5—Acc 50530 W V, a white, male, age 45, with a synovioma of the left thigh five inches above the knee

History—In 1933, the patient first noticed a swelling on the medial surface of his left thigh just above the knee. The tumor at this time was about the size of a half dollar and seemed to be superficial. It grew gradually until two weeks before admission to the hospital when it appeared almost to double its size in ten days. This was accompanied by some pain which radiated down his leg. No history of previous injury could be obtained.

Examination—On the medial surface of the left thigh, five inches above the knee, there was a mass the size of a hen's egg which was firm, warm, somewhat tender, and apparently not fixed to the skin or underlying tissues. Roentgenograms were negative except for soft tissue swelling.

Operation—On June 29, 1936, the tumor was found to have invaded the popliteal space and to surround the femoral vessels. A diagnosis of fascial sarcoma was made and immediate midthigh amputation was performed.

Pathologic Report—*Macroscopic* A large oval, lobulated mass with attached muscle and fat, which measured 11x9x8 cm. The tumor was not well encapsulated and its sectional surface was variable in appearance. Some of the lobules were soft, homogeneous and grey, while others were yellow. No definite cysts were described. The centers of some of the lobules were almost caseous in consistency. *Microscopic* Both typical types of cell are present in the sections studied, but the epithelioid type predominates. So closely packed are they in some places that the usual pattern is missing. Elsewhere, however, a papillary arrangement is presented. In several areas the cuboidal-shaped cells form acinous-like structures which contain pink-staining material. Mitotic figures are frequent and in some areas there are small clumps of foam cells. Where the margin of the tumor is shown, it is obviously invasive.

Subsequent History—The patient has been seen at regular intervals since his operation. At his last examination, January 24, 1939, he complained of pain in his stump, but there was no evidence of local or distant metastases.

Case 6—Acc 40595 C K, white, male, age 17, with a synovioma arising on the left forearm near the elbow.

History—Four months prior to admission to the hospital, the patient noticed a painless swelling on his left forearm that rapidly increased in size.

Examination—A soft, well circumscribed, cyst-like mass the size of a hen's egg which, before operation, was diagnosed as a benign cyst.

Operation—Local excision, June, 1933.

Pathologic Report—*Macroscopic* An irregular lobulated mass which was thought by the operator to arise from a tendon. The tumor was poorly encapsulated. It was yellow in color and contained numerous small cystic areas filled with clear fluid. *Microscopic* The tumor, which is extremely cellular, is composed of interlacing bundles of plump spindle cells. There is a tendency to cyst formations which are lined by a more cuboidal-shaped cell. Conspicuous in some of these small cyst cavities are papillary projections.

Subsequent History—The patient received a short course of postoperative radiation. A year later, June, 1934, a recurrent mass the size of a large cherry was excised. It presented the same pathologic appearance as the original tumor. He has been examined yearly, and, in January, 1939, was reported well, without evidence of local or distant metastases.

Case 7—Acc 43768 E H, white, female, age 35, with a synovioma involving the right knee.

History—Seven years before admission to the hospital, the patient struck the outer surface of her right knee. The area remained sensitive to pressure and a year later a pea-size nodule was noted. There was a progressive increase in size of the tumor ex-

tending into the popliteal space and limiting motion of the knee joint 50 per cent Pain was not an outstanding symptom

Examination—The right knee was one-third again its normal size The enlargement was due to a firm irregular tumor composed of two almost distinct parts, one on the anterior lateral surface and a second filling the popliteal space Fluid also could be demonstrated in the joint Roentgenologic studies were negative for bone involvement and lung metastases

Operation—Biopsy, followed by mid thigh amputation in July, 1934

Pathologic Report—*Macroscopic* The tumor was moderately well encapsulated, almost filling the suprapatellar and popliteal bursae At several points it had invaded the joint cavity The tumor was made up of lobules of rubbery consistency which showed occasional cystic areas No bone involvement could be demonstrated *Microscopic* Sections did not show the typical papillary arrangement which characterized the preceding cases The tumor was comprised of closely packed round or oval cells with little or no visible cytoplasm The nuclei were vesicular with occasional nucleoli In sections from other portions of the tumor, the cells form a lace-like pattern and are more spindle-shaped in character Numerous small blood vessels indicate its vascularity and mitotic figures are quite numerous

Subsequent History—Following operation, the patient had intensive roentgenotherapy, but five months later pulmonary metastases could be demonstrated Her course was rapidly downhill, with death occurring in June, 1938

Case 8—Acc 54821 G S, white, male, age 25, with a synovioma arising in the left popliteal space

History—In July, 1936, three months before admission to the hospital, the patient developed a small lump in the left popliteal region which slowly increased in size The tumor was thought, clinically, to be a bursal cyst and was excised Pathologic report of specimen was "benign cyst" Shortly after operation, the swelling recurred and increased rapidly in size to involve the entire popliteal space He was readmitted to the hospital in December, 1936, because of pain, swelling and loss of motion in his left knee

Examination—Filling the left popliteal space was a firmly fixed tumor which gave the impression clinically in certain areas of being cystic Flexion of the knee was limited to 60° Pressure over the mass produced very little pain Several small nodes were palpable in the left inguinal region There was no evidence of bone involvement roentgenologically

Operation—December 5, 1936, the popliteal region was explored A poorly encapsulated tumor was found which measured 15x7x5 cm and completely filled the popliteal space At one point it appeared to be attached to the periosteum of the tibia The popliteal vessels were completely surrounded by the tumor, which was obviously infiltrating in character, making surgical removal impossible A specimen was excised for study

Pathologic Report—*Macroscopic* No record made *Microscopic* The sections show a cellular tumor made up for the most part of spindle-shaped cells In areas the cells are densely packed and form in whorls, while in others they lie in looser tissue and give a lacey, myxomatous appearance Papillary formation is not striking, but there are cystic areas which are lined by more cuboidal cells Mitotic figures are numerous

Subsequent History—Following operation, the patient's course was rapidly downhill, with death occurring April 16, 1937, four months later At autopsy, metastases were found to the inguinal nodes and both lungs A note on the gross appearance of the tumor at this time is of interest It is described as displaying numerous small cystic areas which contained a sticky, glairy mucoid fluid

Case 9—Acc 58089 A S, white, male, age 27, with a synovioma developing in the left popliteal space

History—Five weeks prior to admission to the hospital, the patient first observed a small lump in the left popliteal space There was no history of previous injury The

tumor steadily increased in size and although there was no real pain, the patient complained of a constricting sensation in this region

Examination—Superficially placed in the left popliteal space there was a fluctuant mass, 5.26 x 3 cm, which was not attached to the skin or the underlying structures

Operation—Excision of cyst under local anesthesia April 21, 1938 There was no apparent communication with the joints

Pathologic Report—*Macroscopic* The cystic tumor is the size of a lemon and contains a chocolate-colored fluid The capsule is 3.4 Mm in thickness, and its inner lining has a sulphur-yellow color *Microscopic* The capsule consists of fibroblastic tissue with numerous small blood vessels and scattered collections of hemosiderin The inner lining is composed of more cuboidal cells varying from three to five cells in thickness Papillary projections are numerous Occasional giant cells of the epulis character are present

Subsequent History—One year following operation, April, 1939, a marble-size tumor developed at the site of the original lesion This gradually enlarged to the size of an egg and, in July, 1939, it was excised The operator again described the tumor as cystic in character Pathologic studies revealed a picture similar to that of the original tumor, but with a greater tendency to papillary formation In February, 1940, the patient reported a second recurrence for which he is now under observation Amputation was refused by the patient He is now receiving radiation therapy

Diagnosis—In none of the nine cases included in this report was a correct preoperative diagnosis made The clinical impression in five cases was benign bursal cyst There is really nothing characteristic about the history or clinical appearance of synovium It is, therefore, of highest importance that detail gross and microscopic pathologic studies be made in all cases of tumors removed from joints or regions adjacent to bursae and tendon sheaths cursory routine examination led two cases to be overlooked by the pathologist, who made the diagnosis of benign bursal cyst The correct diagnosis was not made until a recurrent tumor was explored

In most cases the gross and microscopic appearance of the more common xanthoma or giant cell tumor would quickly differentiate it from synovium Gunnar Jonson,³ in reporting a series of cases treated at the Radiumhemmet, Stockholm, points out the possibility of confusing synovium with a chronic villous arthritis In fact, two of his cases were so diagnosed at operation The more diffuse character of this lesion, together with pathologic studies (Fig 6), should establish the correct diagnosis Whenever a cystic tumor is removed from a region where a bursal cyst may arise and is found to contain chocolate-colored fluid rather than the usual clear gelatinous fluid common to such a cyst, the possibility of a synovium must be considered Should microscopic studies reveal a cellular lining with papillary formations in contrast to the flat single cell lining of a bursal cyst, the diagnosis of synovium is established

Treatment—No dogmatic statement can be made regarding the management of synovium based upon so small a group of cases From a review of the literature one is left with a very pessimistic outlook, regardless of the therapy employed This does not seem entirely justified if we analyze the results of the nine cases herein reported The mortality rate of 45 per cent is misleading if we do not consider that the treatment in three of the four

SYNOVIOMA

RÉSUMÉ OF NINE CASES OF SYNOVIOMA

TABLE I

Case No	Age	Sex	Duration Before Operation	Symptoms	Location	Operation	X-ray Therapy	Results
(1) E D Acc 46896	17	Female	4 months	Soft cystic olive-size tumor	External surface of right ankle	Excision 1933	Yes	Recurrence 1 yr later with inguinal metastases. Death from pulmonary metastases, 1938
(2) E A Acc 37019	45	Female	4 years	A slowly growing moderately painful egg-size tumor	In region of head of left fibula	Excision 1932	Yes	Living and well without evidence of recurrence June 1939
(3) M D Acc 39605	30	Female	2½ years	Swelling with local pain and discomfort on walking	Plantar surface of left foot	Excision 1933	Yes	Recurrence 2 years later. Further X-ray therapy followed by amputation. Death from pulmonary metastases 1938
(4) V S Acc 60073	22	Female	2½ years	Gradual development of painless swelling	Below internal malleolus of left ankle	Excision 1938	Yes	Well without evidence of recurrence 18 months following operation
(5) W V Acc 50530	45	Male	3 years	Gradual swelling with slight pain	Medial surface of left thigh just above knee	Midthigh amputation 1936	No	Living and well 4 years after operation
(6) C K Acc 40595	17	Male	4 months	Painless egg-size swelling	Left forearm near the elbow	Excision June, 1933	Yes	Recurrence 1934. Second excision. Living and well 7 years later
(7) E H Acc 43768	35	Female	7 years	Gradual enlargement of tumor limiting junction of knee	Right knee	Midthigh amputation 1934	Yes	Death from pulmonary metastases 1938
(8) G S Acc 54821	25	Male	3 months	Gradual development of small cystic tumor	Right popliteal space	Excision 1936	No	Extensive recurrence within 4 months and death from pulmonary metastases 5 months later
(9) A S Acc 58689	27	Male	5 weeks	Painless swelling	Left popliteal space	Excision 1938	Yes	Now under treatment for second recurrence

patients who died was totally inadequate. In two of the cases which terminated fatally, the correct diagnosis was not made until the tumor recurred, and even then only local excision was attempted at the second operation, although it must have been obvious that the tumor could not be com-

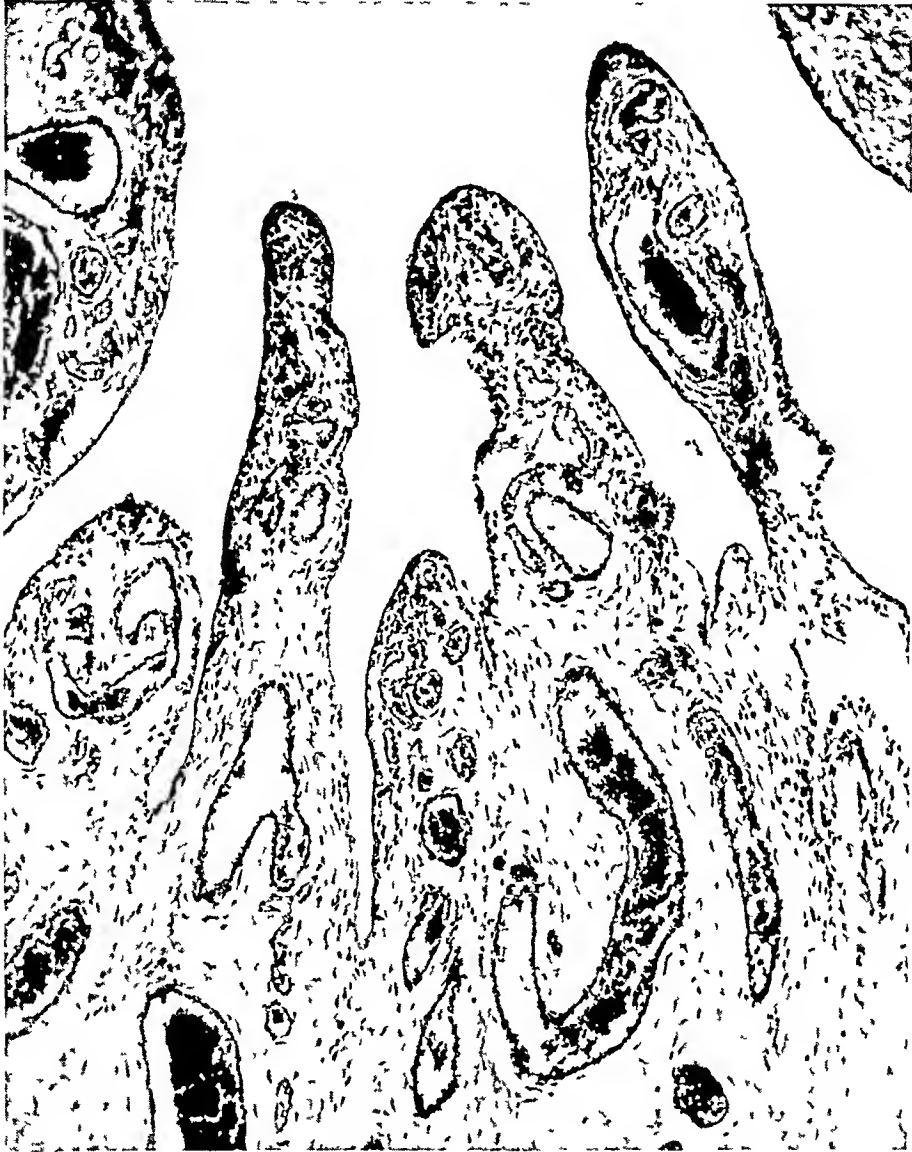


FIG. 6—Photomicrograph to show pathologic pattern of a typical case of villous arthritis

pletely removed without destroying vital structures. A third case, which died, did not seek medical aid until the tumor had grown over a period of seven years from the size of a pea to double the size of the knee. It is not surprising that pulmonary metastases were noted in this instance, five months after a mid thigh amputation. In the fourth fatal case, an incorrect diagnosis of a benign cyst was made at the first operation, and when examined four months later the tumor had already metastasized. This case is unique in this series because of its fulminating course.

Of the five surviving cases, four have been treated by local excision followed by radiation. Three of these are living and well, two, seven and eight years, respectively, after their operation. In the fourth case, two recurrences have developed during a period of two years. The fifth patient is apparently in good health, four years after a mid thigh amputation for a tumor of the popliteal space which could not be completely removed without injury to the popliteal vessels.

We may conclude from the above that the prognosis in synovioma is not as poor as the literature would lead us to believe. Conservative treatment of these tumors along the following lines seems warranted. Whenever the tumor can be completely excised with a margin of healthy tissue and appears encapsulated, this should be the method of choice. Where the tumor cannot be removed completely without injury to important structures, amputation should be performed.

The effect of radiation therapy is, as usual, difficult to evaluate, but it would seem a plausible adjunct to surgery where the tumor has been excised. In this series, however, where inguinal metastases have developed, or there has been a local recurrence, it has not seemed to have had any effect on the ultimate outcome.

Course of the Disease—One conclusion we can definitely draw after a study of these cases is that the rate of growth is slow and metastases appear late in the disease. There was only one exception, the patient who died within nine months of the time when the lesion was first noticed. The other three who progressed to a fatal termination lived five, seven and ten years, respectively, after the onset of symptoms. During the course of the disease three of the four patients who died developed metastases to the inguinal nodes, and at the time of death all showed pulmonary involvement.

CONCLUSIONS

(1) A series of nine cases is reported.

(2) Two distinct types of tumors may arise from synovial-lined structures depending upon what part of the capsule they take their origin. From the outer or fibrous layer, tumors develop which are indistinguishable from the common fibrosarcoma. From the inner or synovial lining of the capsule, cystic tumors may arise which have a characteristic papillomatous pattern. All of the cases of this series fall into this latter group.

(3) Grossly, the tumors may be composed of single or multiple cysts which, microscopically, reveal a typical villous structure of fibroblastic cells covered by cuboidal mesothelium.

(4) In view of the absence of any specific diagnostic clinical features of synovioma, the importance of careful pathologic studies has been stressed.

(5) In the improperly diagnosed and inadequately treated cases, the course is protracted and uniformly fatal.

(6) Based upon a study of the cases of this series and those reported in

the literature, a plan of treatment is proposed which, in the light of our present knowledge, would seem both rational and conservative

I wish gratefully to acknowledge the assistance in the preparation of this paper of Lt Col J E Ash, U S A , Curator of The Army Medical Museum, Washington, D C Upon his pathologic studies, this paper is largely based

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CHOICE OF BONE GRAFT METHODS IN BONE AND JOINT SURGERY

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DURING THE YEARS which have passed since the introduction of modern surgery, many methods of bone grafting have been advocated, each with a plausible explanation of its use. Many of these procedures have not stood the test of time. However, a review of those available to-day reveals a surprising number of useful methods.

There may be wide differences of opinion as to the choice of method to be used under certain conditions, and several may be adaptable. Much depends upon the experience of the individual surgeon with each type of procedure.

There are available, now, for use in bone graft surgery three essential types of graft: (1) Autogenous grafts, in which the bone is removed from one part of the patient and transplanted to another part of the same patient, (2) homogenous grafts, in which bone is removed from another person such as a relative and transplanted to the affected part of the patient, and (3) heterogenous bone transplants, in which bone from another species is used in transplantation. Usually this is some type of beef bone though bones of other animals have been used. These may be subdivided as in Table I.

TABLE I
CLASSIFICATION OF TYPES OF BONE GRAFT

Autogenous grafts

- (1) Cortical bone (usually tibia)
- (2) Cancellous bone (usually iliac crest and wall)
- (3) Osteoperiosteal bone (usually tibia)
- (4) Fibula or rib (combining the foregoing)
- (5) Chip-grafts, shave grafts *etc*
- (6) Delayed grafts

Homogenous grafts

- (1) Cortical
- (2) Cancellous
- (3) Any other type tabulated under autogenous grafts

Heterogenous grafts

- (1) Entire bone
 - (2) Cortical
 - (3) Cancellous
 - (4) "*Os novum*" —combination of heterogenous and autogenous grafts
- } '*os purum*'

There may be variations in the type of graft from the standpoint of its placement at the site of transplant, such as (1) Onlay, (2) inlay, (3) intra-medullary, and (4) wedge—variation of inlay.

In deciding what type of graft is to be used several factors must be taken into consideration.

If the graft is to serve as a fixative agent as well as to furnish osteosynthesis, cortical grafts of some type must be used.

In some instances in which the shearing force may be great and external fixation inadequate, as in ununited fractures of the neck of the femur, a stronger graft than the simple tibial cortical graft may be necessary and a fibular graft may be used. Where such a tubular bone is used, the strength of the graft is much greater and the graft will better withstand the shearing force mentioned.

Where defects in bone are to be filled, as in bone cysts, cancellous bone may be used, although in many cysts the capacity of the defect is such that it is necessary to resort to all the available sources and one may use both cancellous and cortical bone.

Where a definite plastic effect is desired, such as the making of a shelf over an inadequate acetabulum, the cancellous bone from the wall and crest of the ilium seems, to my colleagues and me, to be most adequate.

Where speed of union is important, the cancellous graft of some type is probably the best, for reasons to be demonstrated later, provided it is otherwise suitable.

It may be fairly well shown that all grafts go through certain stages between the time of transplant and the final result, which in many cases is not reached for several months or years after the transplant is done.

Once the transplantation operation is completed, there is about the graft a wall of blood clot which begins the usual stages of organization. During this process blood vessels form in the organizing tissue. If the graft is permeable enough, it may be invaded by the organizing connective tissue. If cancellous bone is used as a graft, this invasion by connective tissue is much more readily accomplished, as may be seen in the experimental grafts. If the graft is a cortical graft with some cancellous bone attached, the invasion by the connective tissue may take place more slowly, and where pure cortical bone is used this invasion is slower in direct proportion to the density of the bone.

After the circulation to the graft is established through the invasion by connective tissue, a stage of reduction in density of the graft begins and in some cases may proceed to such an extent as to make the graft extremely vulnerable. Fractures of grafts during this stage are not uncommon. However, with the completion of this phase and usually by the resumption of some active stress, recalcification and reossification of the graft take place and this process may go on to such a degree that, in the end, the mass of bone over the grafted area is two or three times as large as the original graft.

Hypothesis of Bone Growth—The foregoing observations are taken from a series of experiments reported by Stuck and myself in 1934. At that time we summarized the hypotheses of bone growth into five groups.

(1) Growth and replacement of bone are brought about by specific osteogenic activity of the periosteum (Ollier, 1867).

(2) All of the transplanted bone dies and is replaced by proliferation of new bone from the surrounding host tissue (Baith, 1893).

(3) Replacement of bone grafts and repair of bony defects are effected by proliferation of bone from the periosteum and endosteum (Axhausen, 1908).

(4) The periosteum has no osteogenetic function. Bone grows and repairs itself by proliferation of bone chips (Macewen, 1912)

(5) New bone is formed by metaplasia of the preexisting connective tissue in the region where the bone is to be laid down (Baschkizew and Petrow, 1912)

To this list may be added the views more or less attributed to Leiche and Policard, who stated that "The problem of osteogenesis has passed through many phases. It has been histologic and surgical and at the present time it is, above all, chemical." These authors have elaborated an hypothesis that all formation of bone is the result of metaplastic change in the connective tissue where bone is to be laid down. There are three stages in this metaplasia:

(1) Transplantation of connective tissue by edematous infiltration with multiplication of connective tissue fibrils, (2) infiltration by a special substance clinically undefined, the pieosseous substance, and (3) deposit in that substance of a mixture of calcium phosphate and calcium carbonate, producing bone.

This view may be said to be largely theoretic until more knowledge of chemistry of body tissues and particularly of bone is gained. What such knowledge as the future may bring will do to support or modify this hypothesis is, of course, unknown. But with the rapidly increasing knowledge of chemistry as applied to medicine, it is probably safe to predict that at least a major part of the process of bone formation will be known to be purely chemical.

We have not by any means been able to demonstrate these steps in our experimental work. However, we feel that we have proved that grafts which are more readily permeable by granulation tissue unite more quickly with their host bone. The more compact grafts go through the same process but this takes a much longer time.

Cortical Grafts—My colleagues and I use cortical grafts probably more widely than any other type. In treating ununited fractures of the long bones we use them almost exclusively. Here the splinting effect of a solid graft is most desirable. It is essential to fix the ends of the long bone by some means and fixation can be accomplished in this way. This applies to practically all of the ununited fractures of shafts. Cortical grafts are used as a rule in cases of scoliosis in which the deformity is not severe but in which a supporting graft of the "strut" type is desired. Cortical grafts may be used to fill large defects such as those seen in bone cysts. Bone grafts for tuberculosis of the spinal column and for spondylolisthesis are usually of this type.

Cancellous Grafts—The cancellous type of graft may be used in lumbo-sacral bone graft operations in which only two vertebrae are to be fused, that is, the fifth lumbar vertebra to the sacrum or occasionally two other vertebrae. Such grafts are also adaptable in making shelves in the case of congenital dislocation or subluxation in which a shelving type of operation is desired. Such cancellous grafts are most adaptable in filling small and large bony defects such as are seen in bone cysts or giant cell tumors. In these cases oftentimes a large amount of bone is necessary to fill the defect and it may be necessary to use both cortical and cancellous bone in such instances. Cancellous bone, in

the form either of large flat shavings or of solid grafts from the ilium or trochanter, is often used as an adjunct in the various types of ankylosing operations on the hip

Osteoperiosteal Grafts—In our hands osteoperiosteal grafts are used only in cases of severe spinal deformity, such as are seen in advanced cases of scoliosis or tuberculosis, in which straight or slightly curved solid grafts cannot be made to fit

Fibular Grafts—In our hands fibular grafts are used almost exclusively in cases of ununited fracture of the femoral neck. In these cases the tibial cortical graft has been found to fracture rather late in the convalescence owing to the shearing force noted previously. Although fibular grafts may fracture, such fractures occur much less frequently than in tibial grafts. Another type of fibular graft is the so-called Huntington operation, in which the fibula is transplanted at either end to the remaining epiphyseal portions of the tibia and thus replaces the absent shaft of the tibia

Rib Grafts—Rib grafts have been used over a long period. Many of the earlier workers in bone graft surgery employed rib grafts. In our own experience they are now used for only one type of case, that is, scoliosis with severe deformity of the ribs. In these cases the ribs are resected to correct the deformity as much as possible and used as transplants to reinforce the fusion of the affected portion of the spinal column

It is my impression that rib grafts are used in facial plastic surgery, which is out of our consideration here

Chip-grafts and Shave-grafts—From time to time various authors have recommended the use of chip-grafts and shave-grafts. These are very useful in filling bone cavities, in implanting in the area of fusion in the spinal column or as implants about a site of nonunion to furnish additional bone to the main graft. They usually are obtained from the tibia but also may be obtained from the ilium

Match-grafts—Small pegs of bone used in grafting small fragments of bone together, as in ununited fractures of the carpal scaphoid bone, are often called match-grafts. These are simply small cortical grafts and as such go through the stages of healing seen in any case in which cortical bone grafts are employed

Delayed Grafts—Brooks and Hudson have developed another method of bone transplantation in experimental animals and Key has adapted the method to operations on human beings. In the first stage the transplant is cut on the donor but not removed, and its bed is prepared. In the second stage, several days later, the transplant is removed and placed in its new bed. Key reported the use of this method on patients three times for nonunion with a successful result each time. Leriche and Policard stated that "The take is more rapid and the osteogenesis of better quality. The biologic explanation of this fact is simple. The preliminary preparation leads to a rarefaction of the bone and consequently augments the permeability of the passageways for the rehabilitation."

Along this same line Leriche and Policard quoted the observation of

Chutro "that the bone graft unites better when the transplanted bone is affected by extensive trophic and nutritive disturbances. These disturbances result in a rarefaction which automatically increases the permeability."

These observations are all in accord with what has been noted already, namely, that the permeability of the graft makes for an easier invasion by the connective tissue which becomes the source of blood supply and ultimately is important in the healing and union of the graft.

Homogenous Grafts—From time to time the use of bone from individuals other than the patient has been advocated. In instances in which persistent nonunion has occurred and for some reason, usually because of inadequate size or strength of the bone, the patient's tibia or ilium does not seem suitable as a donor area, grafts may be taken from another individual, usually a parent or close relative, although this relationship is not necessary. That this type of graft may be successful I know from personal experience. I have been unable, however, to obtain from the literature any definite facts regarding the relative success of this type of grafting as compared with autogenous grafting. In one article by Brooks and Hudson on the experimental use of homogenous bone transplants a statement is made that the homogenous graft was successful in 76.8 per cent of cases as against 84.8 per cent of autogenous grafts in the same type of animal. These authors stated that they did not study the reactions in the beds to which the grafts were transplanted. In several of the experiments the blood corpuscles and serums were tested for iso-agglutinins and hemolysins but none were demonstrated. Brooks and Hudson referred to work on transplantation of other types of tissue by Loeb, who found that syngenesioplasmic transplantations were more successful than homogenous transplantations but less successful than autogenous transplants. By syngenesioplasmic transplants is meant the use of transplants from closely related individuals as donors. So far as I have been able to ascertain, this has not been determined from clinical applications of the method.

Neuhof stated that "homoplastic grafting has not had extensive clinical application. Differences between the sera of two individuals is undoubtedly an important factor in the uncertainty of success attending its use, but this has only been considered theoretically and has not been proved experimentally."

Our experience with homoplastic bone transplantations at the clinic has been limited to 19 operations on 14 patients, with the results shown in Table II.

TABLE II

RESULTS OF HOMOGENOUS BONE TRANSPLANTS IN 19 OPERATIONS UPON 14 CASES

	Number of Operations	Success	Failure	Unknown
Donor: Father, mother or brother	13	7	6	0
No relationship	6	3	2	1
Total	19	10	8	1
Blood-matching recorded (cases)*	5		4	1

* Three of these cases were of congenital pseudarthrosis. All donors were parents.

Thus, from our own experience at the clinic it cannot be said that the donor should be a close relative or that the blood should be matched. In one case a piece of bone from a donor not related was preserved in alcohol for a time.

before being used successfully as a graft. Such experiences have been reported in the literature from time to time. Although by no means to be recommended as a routine procedure in bone grafting operations, homoplastic transplantation does have a place in the occasional case in which bone is desperately needed and for some reason or other the patient is in no condition to withstand autotransplantation.

Perhaps more efforts at blood-matching in our series would establish the importance of this procedure, but from these cases studied there is little to offer as an argument in favor of it.

In an emergency one may employ bone from an amputated limb, provided the condition of the amputated part is such that there is no danger in its use. The presence of infection, malignant lesion, *etc.*, would, of course, forbid the employment of such material for grafting purposes. The material may be preserved for a time in alcohol or ether without destroying its value as a graft. One must approach such a procedure without promising too much to the patient, but under conditions of extreme necessity such methods may be used with some assurance of success.

Heterogenous Transplantation—The use of bone from other species than man has been reported from time to time with varying statements of success.⁸ Such materials as beef bone screws, plates and grafts have been employed for many years and are still in rather general use, with perhaps some increased stimulation by the work of Orell which has received widespread publicity during the past few years. Besides advocating the employment of specially prepared beef bone, Orell has recommended the use of what he calls "*os novum*." In this procedure a strip of beef bone is implanted subperiosteally over the anteromedial surface of the tibia. One to two months later the implant together with the newly formed bone surrounding it is transplanted to the desired bed.

The method seems to have gained some popularity, particularly in Europe, if one is to judge by various reports in the European literature. How extensively it may be used in this country I cannot say at this moment. My colleagues and I have used beef bone screws for years. This method of fixation of autogenous grafts has been advocated by Henderson. It has proved a very satisfactory method of fixing grafts. Occasionally there may be some evidence of reaction around the screws and their extrusion may be noted or their removal may be necessary. For this reason my colleagues and I have lately been using vitallium screws to fix our bone grafts. Whether or not they will prove more satisfactory than beef bone screws is as yet to be demonstrated. They have apparently been satisfactory to date.

Beef bone plates were used for some years, usually as a method of fixation of fresh fractures. As such they proved satisfactory in some cases but the fact that they are no longer used attests to the preferability of other means of internal fixation over them.

Other types of heterogenous bone transplant reported in the literature have been bone from rabbits, sheep, chickens and monkeys,¹² eye teeth of

walruses, stags' antlers⁷ and beef horns. This is undoubtedly only a small list of the materials used, as others are recorded in fragmentary case reports such as the successful transplantation of the tibia of a freshly killed goat.⁸ All of this simply shows that again one may, under extraordinary circumstances, employ various types of heterogenous bone as a grafting material. Actually, my colleagues and I feel that the circumstances must be extraordinary to justify the use of heterogenous bone and that for the routine employment of bone grafting methods one should use autotransplants.

Postoperative Complications—Once the transplant is completed, probably the greatest source of failures is through infection. Many rules may be made about the time to operate after all infection has apparently subsided in a compound fracture. Various intervals of from six months to two years—have been advocated as necessary before attempting bone grafting operations. One cannot, of course, ever be sure. It seems to me more important to attempt to determine whether there has been a very active type of infection and, if so, whether there has been serious damage to the surrounding soft parts so that much dense scar tissue is present. One can usually deal with the scar tissue between the ends of the bone fragments by excision. If the soft tissues around the fragments are severely scarred, however, serious impairment to the healing of the graft may result. If infection develops about the graft as the result either of a flare-up of an old infection or of introduction from elsewhere, one must determine, first of all, whether the infection is a localized one, which may cause little or no general reaction, or whether a serious general reaction is taking place. In the latter case, free drainage of the wound may be necessary, combined with whatever general measures may be indicated. In milder, localized infections the utmost consideration must be used in the care of the wound. By such treatment oftentimes a satisfactory union may be obtained and thus a good result salvaged from what may have appeared to be at first a failure. Oftentimes a graft may live in part through such an episode and sufficient normal bone may be formed to promote a good union or whatever effect may be desired from the operation.

Fractures of grafts may occur and, under some circumstances, such a complication may prove serious. This is particularly true where the graft is used to repair an ununited fracture. However, continued external fixation may produce union of the graft through the fractured area and a good result may thus be obtained. In the case of grafts to the spinal column it has been my observation that, as a rule, the strut-graft for scoliosis will unite and be even stronger at the site of fracture. On the other hand, a graft for tuberculosis of the spinal column may fracture and fail to unite, with a resulting failure of the operation. In the former case the constant friction of the ends of the graft may promote union. In the latter case the tendency is for distraction of the ends of the graft to take place with resulting failure of union.

The ultimate fate of grafts, once they are firmly united, is usually to remain *in situ* and, if put to mechanical stress, to increase in size and thickness over two or three years. Occasionally absorption may take place without any

definite known cause, possibly in some instances as a result of a negative calcium balance. In general, the character of cortical bone and cancellous grafts will be maintained.

CONCLUSIONS

- (1) Bone grafts must become attached to the host by granulation tissue.
- (2) This granulation tissue must invade the graft.
- (3) In the case of cortical grafts, this invasion will be delayed because of the relative impermeability of the graft.
- (4) During this period the graft may undergo apparent death of a varying degree of completeness.
- (5) After vascularization the graft may appear to atrophy owing to the increased circulation.
- (6) During this period of transformation and reduced density grafts are more fragile than during other periods and may fracture easily.
- (7) Ultimately both cortical and cancellous grafts become restored to normal consistency.
- (8) Over a period of years most grafts will become thicker and heavier as they are subjected to stresses and strains.
- (9) Dead bone may ultimately become revascularized and replaced by new bone, witness disappearance of beef bone screws in grafts. Sometimes the continued presence in roentgenograms may be an indication of "retarded bone metabolism."

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INTERINNOMINO-ABDOMINAL AMPUTATION *

CASE REPORT

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IN 1935, G. Gordon-Taylor and Philip Wiles¹ published the record of their five cases of hind quarter resection, together with an exhaustive summary of the current literature. Altogether there had been 79 cases reported, with 46 deaths, a mortality of 59.5 per cent. They were able to verify 55 of these cases of which 31 (56.4 per cent) died, of these 55 cases, 37 had been amputated for malignant disease of the lower extremity, with 20 deaths (54.1 per cent), 15 for tuberculosis, with ten deaths (66.6 per cent), one for nontuberculous disease of the hip, which lived, one for osteoclastoma, which was living some five and one-half years later, and one for an unknown cause, which died. Since 1935, 15 cases have been reported in various periodicals in different countries (Table I), of which Gordon-Taylor² has contributed six of his own. Six (40 per cent) of these 15 cases died within variable periods of elapsed time—as long as six months. Of the ones that lived, one had been operated upon five years ago, another three years, three of them for a few months, and of the remainder all we know is that they survived operation. The purpose of this paper is to present the history and subsequent course of a case of successful hind quarter amputation.

The indications for this radical procedure are³

- (1) Extensive disease of the proximal thigh, where disarticulation of the hip will not suffice for complete eradication of the disease. This may be malignant or benign.
 - a. Bone tumors involving the proximal end of the femur, the pelvic bones, or extending into the soft parts of the pelvic cavity
 - b. Chronic bone infections in the same locality not yielding to surgical drainage
 - c. Malignant tumors or infections of the soft parts of the hip area, extending into the bones or into the tissues of the buttocks
- (2) Malignant bone tumors of the ilium and tumors of the soft parts of the pelvis too extensive to yield to local resection of that part, but which require resection of the entire limb
- (3) Extensive dissecting aneurysms of the femoral artery
- (4) Crushing injuries of the hip region, with gas infection
- (5) Tuberculosis of the femur

* Presented before the Academy of Surgery of Detroit, Mich., February 13, 1936

TABLE I
REPORTS OF 15 INTERINNUMINO ABDOMINAL AMPUTATIONS
1935-1941

Surgeon	Date	Sex	Age	Disease	Result	Published
Gersh	1936	M	60	Sarcoma	Died after three months from intercurrent infection	Sovet Khir No 4 681 1936
Shvartz	1938	M	48	Periosteal sarcoma	Died within one month from peritonitis and pulmonary infection	Vestnik Khir 55, 51 Jan 1938
Banet	1936	M	27	Osteosarcoma	Alive at least one month after operation	Bol Liga Contra il Can- cer 11, 43 Feb 1936
Leriche and Stulz	1937	M	23	Ewing's reticulosarcoma	Alive two months later	Mem acad Chir 64, 31 Jan 12 1938
Padovani	1938	M	18	Myeloma	Alive six months later	Mem acad Chir 65, 361 Mar 8 1939
Ricard and Clavel	1938	M	36	Osteosarcoma	Died same day	Lyon Chir 35, 81 Jan 1938
Pascalis	1936	M	44	Osteosarcoma	Survived operation	Progres Méd 39, 1481 Sept 26 1936
Gordon-Taylor	1935	M	17	Spindle cell sarcoma	Living five years later	Brit Jour Surg 27, 643 April 1940
	1936	F	37	Osteolytic sarcoma	Died three hours after operation	
	?	F	25	Spindle cell sarcoma	Living three years later	
	1938	M	14	Osteosarcoma	Died six months later from metastases to spine	
	1938	M	34	Spindle cell sarcoma	Died 20 hours after operation from shock	
Rapant	1939	M	26	Chondrosarcoma	Survived operation	Chirurg 10, 804 Nov 15 1938
	1937	M	29	Osteolytic sarcoma	Survived operation	
	1937	M	14	Osteolytic sarcoma	Survived operation	

Certain rules are accepted in selecting this operation. If, after complete physical examination, a malignant tumor is found, careful search must be made for local and distant metastases, especially to the lungs and thorax. The disease should not have penetrated into the pelvis nor beyond the boundaries of the sacro-iliac joint and symphysis pubis. The patient should be a reasonable risk, and should understand that he risks his life in the hope that he will be relieved from the disease or pain he suffers.

Since these rules were first laid down, the recognition of the importance of a transfusion administered during the operation has greatly lowered the mortality, and the patient can approach the operation with greater probability of recovery.

Case Report—C B, white, male, age 40, reported to another hospital, December 31, 1934, complaining of a sprain in the right leg, the result of recent heavy lifting. Physical examination revealed an inflamed mass in the right proximal thigh, accompanied by general malaise, chills, and fever. He returned to work after symptoms had subsided, only to be incapacitated a short time later by a recurrence of symptoms. In February, 1935, the mass was aspirated but nothing was obtained, it was removed locally after signs of inflammation had subsided. The patient felt better, gained ten pounds in weight, and returned to work.

He remained symptom-free until August 5, 1935, when he was referred to us because of a large, stony-hard, nonfluctuant mass in the anterior right thigh, and a loss of 30

pounds in weight. A specimen was taken for biopsy under light general anesthesia. The tumor was 5 cm in diameter, partly fibrous in appearance, nonencapsulated, with necrotic center and some blood. Microscopic examination revealed extensive necrosis with small islets of spindle cell sarcoma surrounding the blood vessels. The pathologist believed that the tumor had not metastasized, and if completely excised would probably not recur. He was hospitalized for further observation with this end in view.



FIG. 1—The medial aspect of the resected right lower extremity, showing tumor

Roentgenologic examination revealed a marked soft-tissue swelling of the right thigh, there was no evidence of involvement of the bony structure except a slight pressure deformity in the shaft of the femur below the lesser trochanter. *Laboratory Data* Negative Kahn, negative urine, no Bence-Jones bodies, R B C 2,880,000, with 40 per cent hemoglobin, W B C 17,000, with 91 per cent polymorphonuclears and 7 per cent lymphocytes. His blood was Type II, and donors were readily found among the family.

With the object of preparing the patient for an interinnomino-abdominal amputation, he was given preliminary roentgenotherapy,* divided into three doses, one on September 25, another on September 26, and a third on September 27, and, in addition, he was given 350 cc of whole blood on the first day and 400 cc on the second.

* The deep therapy consisted of the following dosage

August 25, 1935—Right thigh, Machlett 1, Cone 2, 200 KV, 1.5 Mm cu, 1 Mm al, 50 cm std, 20 ma, 30 min, 600 ma, 100 per cent SUD

August 26, 1935—Right inguinal region, ant, same technic, 55 cm std

August 27, 1935—Outer aspect upper third right thigh, same technic

Following the roentgenotherapy the patient was very weak and slightly delirious, but after the biopsy incision, which permitted drainage of the straw-colored contents, the toxemia lessened, he gained strength, became rational, and on September 30, 1935, the interinnomino-abdominal amputation was performed.

Operative Procedure—Under spinal anesthesia, the patient was turned a little to the left side by means of sand bags, and, with careful attention to hemostasis, the incision



FIG. 2.—The lateral aspect of the resected right lower extremity.

was made along the iliac crest, down through the inguinal region well above the site of the tumor, and carried to the inner side of the thigh to form a large posterior flap. The upper edges of the wound were then dissected onto the lower abdominal wall, the inguinal canal exposed, the external ring divided, and incision made medially to divide the attachment of the rectus muscle. The external oblique fascia was separated parallel with the inguinal canal as far as the anterior iliac spine, the muscles of the abdominal wall were divided at their insertion on the iliac crest, and the incision carried backward to the posterior superior iliac spine. The internal oblique was pushed up from Poupart's ligament exposing the external iliac vessels. The external iliac artery and vein were encircled separately by a heavy silk ligature and held by clamps, so that in case it became necessary to terminate the proceedings before completion of the operation, the blood supply to the lower extremity could be resumed.

The incision was next carried down on the posterior inferior iliac spine, well away from the genital crease, down the thigh, posteriorly and around, to connect with the anterior incision, thus forming a large flap on the inner side. The gluteal muscles were partially divided, and the tissues freed from the greater sciatic foramen. The inferior gluteal artery was ligated, the psoas muscles divided, and the posterior portion of the ilium exposed.

The ilium was divided just lateral to the sacro-iliac joint, the division extending toward the greater sciatic foramen, a forceps was placed in the foramen, a Gigli saw was drawn through, and another forceps inserted from above—beneath the muscles covering the inner surface of the ilium—to grasp the saw and bring it up to the superior border. The bone was then divided completely with the saw.

After the ilium was divided and drawn outward, the sacral plexus was exposed, then the nerve trunks were injected with 2 per cent novocain, all nerves cut, but the iliac vessels were not exposed. The abdominal contents, covered by peritoneum, were freed from the soft tissues covering the ilium, and held mesially by manual retraction. The symphysis and adherent tissues posterior thereto were divided more completely, the spermatic cord being held well out of the way to avoid injury. The right side of the pelvic ring and the lower extremity were removed, the vessels ligated, and the flaps sutured with silk-



FIG 3—Roentgenogram of the pelvis after resection of the ilium, ischium and pubis on the right side

worm gut. Careful approximation of the flaps was not attempted as the blood supply was considered more important. Three cigarette drains were inserted beneath the flaps and dressings applied.

The anesthetic consisted of 15 mg (0.25 gr) of novocain and 45 mg (0.75 gr) ephedrine dissolved in spinal fluid. It was administered at 11 57 A M, the first incision was made at 12 05 P M, at 1 P M nitrous oxide and oxygen were added and transfusion begun. The operation ended at 1 30 P M. Pulse and blood pressure were normal throughout. The patient was returned to the ward in good condition, warm blankets were applied, and a second transfusion administered later in the day.

Subsequent Course—From Figures 3, 4 and 5 it will be seen that an uneventful recovery ensued. The edges of the flap sloughed away, producing a clean granulating surface, which was covered by epithelium in a few weeks. The patient was discharged December 19, 1935.

Two months after discharge from the hospital the patient was placed in the hands of a prosthesis maker to solve the problem of providing support in the absence of one-half of the pelvis. There had been a gain in weight and an absence of pain. On March 2, 1936, a small nodule appeared in the skin flap and microscopic examination showed this to be spindle cell sarcoma.

This return of a sarcomatous growth in the skin flap, even though the sarcoma has been widely excised, is quite common, and such recurrences have been frequently reported.

On March 10, 1936, the patient was readmitted to the hospital for roentgenotherapy and, on March 26, 1936, generalized convulsions lasting a few minutes developed, followed by difficulty in speech and motor involvement of the right upper extremity. The con-

vulsions continued and the patient died, April 2, 1936 The cause of death being due to spindle cell sarcoma with intracranial metastases



FIG 4—Posterior view of patient with completely healed hind quarter resection

FIG 5—Front view of patient with completely healed hind quarter resection

SUMMARY

A brief review of Taylor and Wiles'^{1 2} survey, with a review of the current literature on reports of interinnomino-abdominal amputation since 1935, has been presented

The case of a white male, age 40, with a spindle cell sarcoma of the right thigh is reported A description of the procedure for a complete hind quarter resection is given The importance of careful preparation for operation, and the administering of a transfusion during the operation is emphasized

The patient recovered from the operation but died six month later of intracranial metastases

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AN OPERATIVE TREATMENT FOR RECURRENT DISLOCATION OF THE SHOULDER

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A REVIEW of the literature on the operative treatment of recurrent dislocation of the shoulder reveals that there is practically no other orthopedic condition for which so many differing operative procedures have been devised. This, in itself, indicates a lack of unanimity of opinion as to the value of these procedures. This is in part due to the lack of opportunity for intensive numerical experience because of the relative infrequency of this condition. One thing is evident from this review, that the simplest procedures are the most popular.

The operative technics usually employed fall into two major groups: (1) Those which aim to repair the cause of the recurrent dislocation of the shoulder, and (2) those which attempt to prevent the recurrence of the dislocation regardless of the causative factor. It is not the purpose of this presentation to review all of the operative methods devised for this disturbance. I shall merely restrict myself to those groups of procedures which utilize the long head of the biceps tendon as a suspension apparatus for the head of the humerus in order to prevent the recurrence of the displacement.

The advantages of the use of the long head of the biceps are: (1) It makes possible the construction of an arrangement similar to a strong ligamentum teres in the hip, (2) it is available at the site of the operative procedure, and (3) it eliminates the necessity for additional incisions to obtain fascial or tendon transplants.

In 1926, Rupp¹ expressed the belief that the long head of the biceps was the causative factor in the recurrence of the dislocations because of pressure on the head of the humerus in downward and outward directions on certain motions of the arm. He, therefore, unwittingly made a suspensory apparatus out of the long head by suturing it to the capsule and periosteum of the humerus. The results of this procedure were not very satisfactory because, in all probability, a firm tendo-osseous union was not obtained in most of his cases.

Heymanowitsch,² in 1927, described two variants of a suspension procedure. In the first variant, he freed the whole biceps tendon and severed its origin at the upper rim of the glenoid. He then drilled a hole through the head of the humerus and threaded the freed tendon through this bone channel and fixed the proximal end to the acromion. In the second variant, he cut the tendon at the level of the surgical neck of the humerus, drilled a channel as previously, through the head of the humerus, threaded the proximal portion of the severed tendon through the channel, and reunited the cut ends of the biceps tendon.

In 1929, Nicola³ described an operation, independently of Heymanowitsch, which is identical with the latter's second variant. Nicola's description popularized this method in this country.

In 1933, Roberts⁴ described an operation in which the long head of the biceps was buried in a deepened bicipital groove. Burnet's⁵ achieved remarkably good results with this method.

The Heymanowitsch-Nicola procedure, though relatively simple, presents certain practical objections and technical difficulties. This procedure neces-

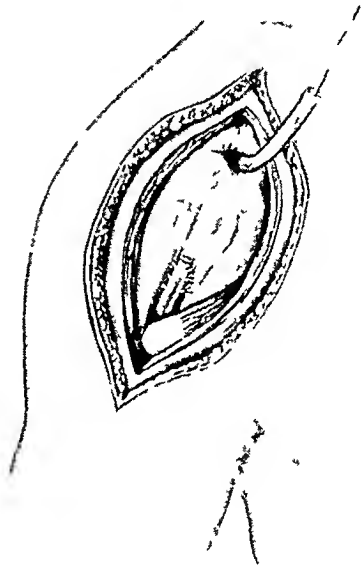


FIG 1—Showing the proximal part of the cut tendon of the long head of the biceps lifted out of the bicipital groove. The distal end is fixed to the periosteum.



FIG 2—Showing the proximal part of the cut tendon pulled through the bone channel in the greater tuberosity of the humerus, and fixed snugly to the surrounding tissue.

sitates the opening of the scapulohumeral joint, thus exposing it to unnecessary trauma and involvement in the event of an untoward infection with the possible dire after-effects. Technically, the drilling of the channel and the threading of the tendon through the channel may at times be difficult, necessitating considerable manipulation and trauma to the joint cartilage as well as to the tendon, and prolonging the operation. Furthermore, improper placement of the channel may result in recurrences. To overcome these objections I^{6, 7} have described, in 1931, a simpler, safer and more certain procedure (Figs 1 and 2).

Operative Technique—This consists of a three-inch long, longitudinal skin incision starting just below the medial border of the acromion and overlying the bicipital groove. The deltoid muscle is split longitudinally by blunt

dissection and if the groove does not present itself in the operative field it can be brought into view by rotating the arm internally or externally. The sheath of the long head of the biceps is incised and the tendon is freed from the sulcus. About one inch above the muscular portion of the long head of the biceps, strong silk sutures are placed fixing the tendon to the periosteum while the forearm is held in 45° flexion. A stay suture is placed immediately above the fixation sutures. The tendon is cut below the stay suture and is lifted out of the bicipital groove. A drill hole measuring about one-half to three-quarters of an inch in length is made extending from the bicipital groove through the greater tuberosity. The free end of the cut tendon is then scarified and threaded through this channel while the arm is held in 45° abduction. The tendon is snugly fixed to the periosteum and the surrounding tissues with strong silk sutures. The wound is then closed and the extremity is immobilized in a plaster of paris spica in 45° abduction or in a Velpeau bandage for a period of three weeks. On removal of the bandage the patient usually presents a complete range of motion. Several weeks of physiotherapy complete the after-care.

In addition to my⁶ four cases, published in 1931, I have employed this procedure on ten other patients, making a total of 14 cases. Of these, 11 were males and three were females. Nine were laborers, and the others had less strenuous occupations. One of the laborers was an epileptic. Twelve of these patients were under my personal observation for three to six years, one for one year and nine months, and another for one year. All of these had had frequent dislocations of many years' standing, at times on the slightest motion of the arm or the slightest exertion such as sneezing or coughing. The above mentioned epileptic sustained, during a seizure, a fracture of the olecranon of the same extremity 11 months subsequent to the operative procedure without redislocating his shoulder. Another of these patients had had a previous partial excision and reefing of the capsule, with subsequent recurrence of the dislocation. All of these patients regained a full range of painless motion subsequent to my operative procedure, and all of them returned to their previous occupations without any disability whatsoever. None have had a recurrence.

Anschutz,⁸ Heyn,⁹ and Jungling¹⁰ have employed this procedure in six instances. These were followed over a period of six months to over two years. Only one of these reported cases had a recurrence, which occurred at the end of the second year, under circumstances which were not disclosed.

Eleven other cases are known through personal communications with three surgeons^{11 12 13} who observed them for a period of over two years. None of these patients sustained a recurrence.

Altogether, 31 cases, known to me, have had the above described procedure for recurrent dislocation of the shoulder. Twenty-eight of these have been observed for two to six years. Only one of them has suffered a recurrence of the dislocation.

SUMMARY

(1) This communication describes additional experience with a simple, safe and effective operative procedure for recurrent dislocation of the shoulder

(2) Thirty-one known cases have been followed by the author and other surgeons, with only one recurrence

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SUBTALAR DISLOCATIONS

CASE REPORT OF THE INWARD TYPE

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WITH the intense interest shown during recent years in the treatment of fractures, it is surprising that the study of dislocations has been neglected. Some of these injuries may test to the utmost the anatomic knowledge and ingenuity of the surgeon if they are to be clearly understood and successfully treated. This is particularly true of subtalar dislocations of the foot, for, when such a condition is encountered, even after careful study of the roentgenograms, it is often difficult to understand its true nature and to institute proper treatment.

A subtalar dislocation is a rare traumatic injury of the foot in which the calcaneus and navicular are displaced, the talus retaining its normal position within the ankle mortise. The displacement of the foot upon the talus can be inward, outward, backward or forward. Baumgartner and Huguier² collected all recorded cases up to 1907, and Shands²⁶ made an additional collection to 1927.

It is the purpose of this paper to report a case of subtalar dislocation of the *inward* type and to discuss the pathology and treatment of this unusual and interesting injury. The literature has been reviewed and a résumé made of case reports since Shands' collection of 1927.

Case Report—J. J., Negro, male, age 52, was admitted to Knickerbocker Hospital January 25, 1940. He stated that he slipped while walking on an ice-covered pavement, his right foot turning inward, became caught in a depression in the ice and he fell forward across his fixed foot. When attempting to rise, he felt severe pain in his right ankle and noticed that his foot was fixed in an inverted position.

Physical Examination The right foot presented an astonishing deformity (Fig. 1), it was markedly inverted, plantar flexed and displaced inward. The inner border of the foot was elevated, the outer border depressed and the plantar surface faced the opposite foot. On the outer side of the foot the lateral malleolus was unusually prominent, and anterior to it was a large immovable bony mass, identified as the head of the talus, over which the skin was tightly drawn, smooth and tense. The body of the talus could be palpated on the dorsum of the foot, in its normal relation to the tibia, and slight active flexion and extension of the foot at the ankle was possible. No active or passive inversion or eversion was possible, the foot being held in its abnormal varus position as in a vise. There was considerable swelling about the foot and ankle but the skin was unbroken.

Roentgenograms (Figs. 2, 3, 4) revealed a subtalar dislocation of the inward type.

Treatment One hour after the injury, under cyclopropane-oxygen anesthesia, closed reduction was accomplished. **Manipulative Technique** With the knee flexed in order to relax the tendo Achilles, the foot was grasped with the left hand under the heel and the right hand about the metatarsal region, and while steady traction was applied downward in the axis of the leg, the foot was placed in dorsiflexion and everted, as an assistant exerted pressure on the head of the talus. As reduction took place, there was a sharp report which could easily be heard across the room. A plaster casing was applied from

the toes to the tibial tuberosity, the foot being held at a right angle with the leg and neutral to inversion and eversion. Examination and roentgenograms (Figs 5, 6, 7) showed that satisfactory reduction had been obtained.

After Care The casing was removed four weeks after reduction and active motion of the ankle and foot was encouraged. Light weight-bearing was started six weeks, and full weight-bearing seven weeks after the injury. Normal range of subtalar and ankle motion returned rapidly, and ten weeks after the injury, the patient walked without pain or limp, and had returned to work.



FIG 1—Before reduction, showing inversion of the foot and prominent head of the talus

The first reported case of subtalar dislocation was by Hey,¹⁴ in 1810. Before this time the condition was confused with midtarsal, complete talar and ankle dislocations. Cases were reported by Judcy¹⁵ and Dufaurets,⁹ in 1811, and by Sir Astley Cooper,⁶ in 1815. Nelaton,²⁰ in 1835, described a dissection of a typical case of the outward type, and, in 1847, gave a detailed description of the injury in his *Pathologie Chirurgicale*. Wells,²⁰ Arnott,¹ McDonnell,¹⁷ and Hancock,¹³ made early contributions in case reports.

Broca,⁴ in 1852, in an outstanding paper, analysed all reported cases, gave the name subastragaloid to the dislocation and described the inward, outward and backward types. He demonstrated that the talus retains its normal relationship in the ankle mortise and that the navicular and calcaneus,

together with the other tarsal bones, are displaced. Malgaigne,¹⁸ in 1855, described the forward type but considered the talus the dislocated bone and, reversing the nomenclature of Broca, classified the types according to the position of the head of the talus. Broca's terminology is universally used to-day, the types of the dislocation being classified according to the position taken by the foot and not that taken by the head of the talus.

Quenu,²² in 1883, described a dissection of a case of the inward type, analysed the causes of irreducibility and wrote on the treatment of all the types. In 1907, Baumgartner and Hugueni,² in a remarkable treatise, collected all case reports in the literature, described the mechanism and pathology



FIG 2—AP view of the ankle, showing medial displacement of the foot at the subtalar joint. Note normal relationship of the talus in the tibiofibular mortise.



FIG 3—Oblique view of the foot and ankle showing disruption of the talonavicular joint.



FIG 4—Ventrodorsal view of the foot showing the head of the talus lying over the calcaneocuboid articulation.

after experimental production of the dislocation and discussed the treatment of the various types. This paper and that of Broca are classics in the literature of the subject. Reismann's²⁴ report, in 1907, analysed the mechanism of the injury and described in detail the anatomy and physiology of the subtalar joint. Thienhaus,²⁸ in 1907, Moore,¹⁹ in 1922, and Shands,²⁶ in 1927, have written excellent papers in English.

Pathology In typical dislocations of the *inward* type, the head of the talus is completely separated from the navicular and lies at the lateral side of the foot on the superior surface of the cuboid. The extensor tendons are medial to, and the cruciate cicular ligament beneath, the head of the talus. The calcaneus is displaced inward. Ligamentous damage is extensive with rupture of the dorsal talonavicular, the interosseous talocalcaneal, the anterior and lateral talocalcaneal and the anterior talofibular ligaments. Rupture of the powerful interosseous talocalcaneal ligament is essential to the production of the dislocation. In the *outward* type, the head of the talus lies on the medial side of the foot in relation to the inner surface of the navicular, while the calcaneus is displaced outward. In the *backward* type, the calcaneus is displaced backward and the head of the talus rests upon the superior surface

of the navicular In the *forward* type, the calcaneus is displaced forward and the head of the talus rests upon its superior surface

Compound dislocations with protrusion of the head of the talus occur frequently Dehoey⁷ collected 26 compound dislocations of all types Necrosis

FIG 5



FIG 7



FIG 6



FIG 5—After reduction

FIG 6—After reduction lateral view of the foot and ankle

FIG 7—After reduction AP view of the foot showing normal talar-navicular articulation

of the skin tightly stretched over the head of the talus, resulting in a compound wound, occurs as a complication of late reduction In Larget's¹⁶ case, skin necrosis developed four hours after the injury

A careful search of the literature reveals ten cases of subtalar dislocation reported since Shands' collection in 1927 There are seven dislocations of the inward type and three of the outward type, three are compound and two have associated fractures A short synopsis of these case reports is appended

REPORT OF TEN CASES OF SUBTALAR DISLOCATION

From the Literature Since 1927

Case 1²⁵—A female, age 40, getting off her bicycle stepped in a hole in the street Examination showed the left foot to be fixed in inversion The head of the talus was prominent on the outer border of the foot Roentgenograms showed a subtalar dislocation of the inward type

Treatment—Closed reduction

Result—Normal ankle and foot movements

Case 2²⁵—Male, age 47 While riding a bicycle, the patient was struck and run over by an automobile. Examination showed the left foot to be in extreme supination. The skin on the lateral aspect of the dorsum of the foot was tightly stretched over the prominent lateral malleolus and the head of the talus. Roentgenograms showed a subtalar dislocation of the inward type.

Treatment—Closed reduction

Result—Normal foot and ankle movements

Case 3²¹—Male, age 39, jumped into a trench. Examination revealed the left foot to be fixed in a marked varus position. There was a large, dirty wound on the lateral aspect of the foot through which the head of the talus and the lateral malleolus protruded.

Treatment—Astraglectomy

Result—Excellent functional result, with motion at the new tibiotarsal articulation

Case 4⁵—Female, age 72, fell on her inverted right foot into a pit three feet deep. The foot was immobilized in plaster without reduction. One month later roentgenograms showed that reduction had not been made and examination revealed the foot to be fixed in marked supination and plantar flexion. The head of the talus was prominent on the outer border of the foot. Roentgenograms showed a subtalar dislocation of the inward type.

Treatment—Closed reduction with the aid of an Esmarch bandage

Result—Normal foot and ankle motions

Case 5¹⁰—Male, age 35, while pushing on the foot brake of his car, crashed into the rear of a truck. Examination showed the foot to be in marked inversion with slight plantar flexion. There was a prominence in the region of the lateral malleolus. Roentgenograms revealed a subtalar dislocation of the inward type with a fracture of the body of the talus.

Treatment—Closed reduction

Result—Complete return of joint function

Case 6²³—Male, age 53, slipped from a stepladder and fell to the floor. Examination showed the typical findings of a subtalar dislocation of the inward type.

Treatment—Closed reduction

Result—Normal motions of the foot and ankle

Case 7³—Male, age 39, slipped off a chair falling on his left ankle. Examination. The left foot was fixed in an equinovarus position. The lateral malleolus was prominent almost piercing the skin and the head of the talus presented at the outer aspect of the foot. Roentgenograms revealed a subtalar dislocation of the inward type.

Treatment—Closed reduction

Result—Complete return of joint function

Case 8²³—Female, age 20. The patient fell six feet from a trapeze, landing on her right foot. Examination revealed the right foot to be in an exaggerated pronated position. The head of the talus protruded through a wound on the inner side of the foot, below and anterior to the medial malleolus. The tendon of the *tibialis posterior* was seen in the wound, lying on the superior surface of the head of the talus preventing reduction.

Treatment—Debridement and open reduction

Result—There was complete loss of subtalar motion, but ankle motion was within normal range.

Case 9¹²—Female, age 62, tripped on the metal guard of a street car step and her left foot came down forcibly on the step below in a pronated position. She noted that her foot was turned markedly outward. Roentgenograms revealed a subtalar dislocation of the outward type with associated fractures of the cuboid and lateral malleolus.

Treatment—Closed reduction

Result—There was 50 per cent limitation of inversion and eversion of the foot.

Case 10¹¹—Male, young, received a blow on the outer surface of his right foot at the level of the lateral malleolus. Examination showed a large wound on the inner side of the foot, extending from the medial malleolus backward to the *tendo Achilles*. The foot was rotated so that its plantar surface presented outward, with its inner border depressed. The talus retained its normal relationship with the ankle mortise.

Treatment—Debridement and open reduction

Result—Normal ankle motion. There was considerable limitation of inversion and eversion of the foot.

Treatment In simple, early cases, closed reduction is usually readily accomplished by traction and manipulation—the method of reduction depending upon the type of dislocation under treatment. General or spinal anesthesia is necessary, and the knee should be flexed in order to relax the calf muscles.

Inward Type Reduction is obtained by traction downward in the axis of the leg and the foot is dorsiflexed. As pressure is exerted on the head

of the talus, the foot is everted. If sufficient traction cannot be obtained by grasping the foot, a Kirschner wire through the calcaneus will make a more powerful pull possible.

Outward Type Reduction is performed by similar downward traction, the foot being inverted as pressure is exerted on the head of the talus. Cases of this type, in which reduction is prevented by the tendon of the tibialis posterior, may be successfully reduced, at times, if the foot is forcibly dorsiflexed in order to relax this tendon.

Backward Type Reduction of dislocations of this type is accomplished by the method described by Destot.⁸ The foot is forced into extreme plantar flexion and, as forward traction is placed on the calcaneus, the head of the talus is pressed into its normal relationship with the navicular.

Forward Type Broca's⁴ case is the only one in the literature in which closed reduction was successful. He applied downward traction on the foot to disengage the calcaneus from beneath the talus and then pulled the foot backward. Cases of this type reported by Thienhaus²⁸ and Smith²⁷ were old and both required open reduction.

Arthrotomy is indicated when closed reduction is unsuccessful. The incision is made directly over the prominent talar head and the cause of the irreducibility is removed. The cruciate crural ligament, drawn tightly about the head of the talus, is the most frequent cause of unsuccessful reduction in dislocations of the inward type. The tendon of the tibialis posterior, lying upon the neck of the talus and between it and the navicular, frequently makes reduction impossible in dislocations of the outward type. Division of this tendon may be necessary.

Late, unreduced cases, in which treatment has been delayed and degeneration of the articular cartilage has developed, are best treated by talocalcaneal and talonavicular arthrodesis after open reduction, as suggested by Wilson.³⁰ However, Clavel's⁵ case (Case 4), which was unreduced for four weeks, demonstrates that a good result may be obtained in a late case by simple, closed reduction.

Compound subtalar dislocations were formerly treated by excision of the talus. With the development of better methods of handling compound wounds, these injuries can now be safely treated by careful débridement, reduction and immobilization. Excision of the talus should be reserved for late, infected cases, and for those associated with a badly comminuted fracture of the talus.

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THE THIRD PHASE OF SURGERY

TOTAL STERILIZATION AS A BASIS OF INTEGRAL ASEPSIS AND OF PASTEURIAN CICATRIZATION

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THE THREE PHASES

THE fact which strikingly dominates the evolutionary history of surgery is that of the battle of the surgeons against the infection of surgical wounds

With respect to the fundamental phenomenon of the healing of the operative wound, this battle can be clearly divided into three periods

The first phase, which has lasted for centuries, is characterized by the ignorance of the existence of microbes

This was the period of "healing by secondary intention" the systematic suppuration of the wound, with its terrible consequences—septicemia, pyemia, gas gangrene, tetanus, *etc*

The second phase makes its appearance with the first notions of the existence of bacteria, it is characterized by the possibility which the surgeons have had to control partially, by means of the methods of Lister and of Terrier, the action of bacteria on the operative wound It is further characterized by the appearance of "healing by primary intention," in direct relation with surgical results which are extraordinary in comparison with those of the preceding period

Without looking more closely at the reverse of the medal, and despite the statement of Pasteur in 1865 "I shall have to fear only the germs of the air, suspended around the patient's bed," one eris in believing in healing by primary intention on the basis that the wounds eventually may show no contamination

Nevertheless, to such an extent was this belief held, that when, in July, 1935, I stated before the Surgical Academy of France "We knew healing by primary intention only under its septic aspect, necessarily followed by an inflammatory reaction," although representing the truth, the Academy considered this to be heresy, and stated in order to safeguard its responsibility "The office wishes to point out that the authors fully retain the responsibility for their writings"

Everyone should nevertheless know that healing by primary intention takes place, as I have already remarked, in the mouth, the nose, the intestine, the anus, *etc*, *ie*, in a septic medium The constant contamination of the operative wound which heals by primary intention is an incontrovertible fact One always operates with instruments and material which are contaminated after having been carefully sterilized in the autoclave To demonstrate this fact one has only to cover the surgical equipment with agar and expose it

to the air in an operating room. After incubation, numerous bacterial colonies are found to be present (Fig. 1).

However, it is hardly necessary to go out of one's way to this extent, since we all know that chasing flies in the operating room is part and parcel of the so-called aseptic operative procedure, a fact to which I believe I first

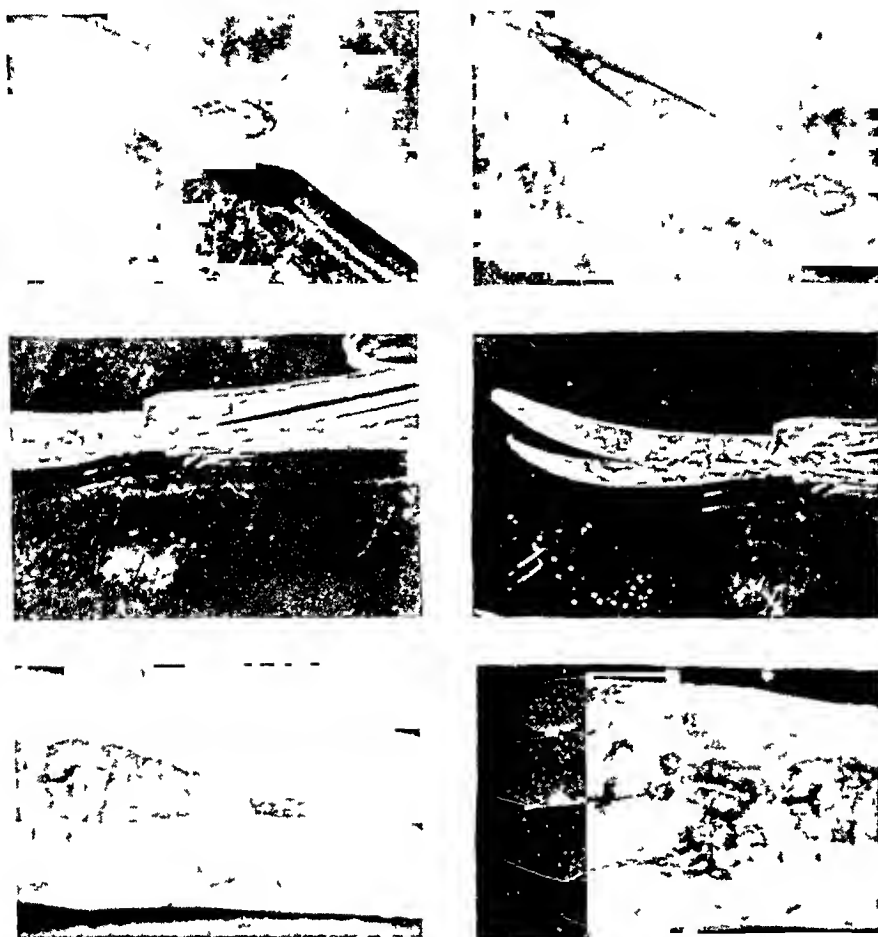


FIG. 1—Bacterial colonies growing on surgical equipment which was sterilized by autoclave, covered with agar, and exposed to the air in an operating room.

called attention in a paper entitled "Aseptic Method and Fly-Tennis" but, as I discovered later, it had already been commented on by others.

The inflammatory reaction of the wound is visible to the naked eye through redness, edema, and the existence of bacteria in the seropurulent droplets situated where the sutures enter and leave. This contamination is easy to demonstrate bacteriologically and by means of sections which reveal the existence of bacteria in the depths of the tissues.

Furthermore, when the operative wound is reopened during the course of cicatrization—and we are referring now to wounds which are healing by primary intention—one observes a purulent appearance of the healing tissue.

Healing by primary intention is in reality a state of unstable equilibrium which is the consequence of phenomena of infection. On the one hand, we have the contamination of the operative wound (quantity, character, and

degree of virulence of the bacteria), and on the other hand, the defensive reaction of the organism (general and local immunity)

At the present time, these facts completely escape our attention

Because of these facts, healing by primary intention evolves, unpredictably, either in the direction of its completion or in the direction of suppuration, *i.e.*, secondary intention, or more serious complications

Healing by primary intention must, therefore, be regarded as the healing of a contaminated wound, the closure of which takes place by direct juxta-



FIG 2—This cut is reproduced from the book *Intracranial Tumors* By Professor Bailey of Chicago. One sees a nurse hunting flies during the operation! The cut antedates (1933) the one which I published in 1936 in my paper *Aseptic Method and Fly Tennis*

position, and which is in general characterized by (1) An inflammatory reaction, (2) the fact that hematomata suppurate readily, (3) a marked lack of tolerance for foreign bodies which remain in the organism, (4) the more or less frequent necessity of drainage, *i.e.*, of an evacuating agent which is at the same time a contaminating agent

In practice, it is important to know the result of this permanent and inevitable state of contamination of the operative wound by an aseptic method associated with the presence of bacteria, a method which contains a fundamental source of error

It is quite obvious that a postoperative period based on this state of unstable equilibrium requires constant vigilance, because of the possibility of accidents

I believe I am justified in stating that 90 per cent of what is called the postoperative illness is merely due to infection

In a summarizing review presented before the Surgical Academy of

France on the tenth of July, 1935, and based on the recent statistics of surgeons in all countries whose quality and capacity are beyond doubt, I have called attention for the first time to the long and impressive series of operative accidents and incidents based on the fundamental fact of the permanent contamination of the operative wound. I have reinvestigated all the sources of contamination—the patient's skin, the surgical equipment, the atmospheric air—and I have shown that, in the present state of surgery, it is the contamination of the air to which must be attributed the great majority of these accidents. These accidents run the gamut from a simple extrusion of sutures to the death of the patient.

We have to deal with suppuration, evisceration, and evisceration as a result of the rupture of the body wall, with failures in the cure of eventrations, with peritonitis, with osteomyelitis and arthritis in bone surgery, with empyema in thoracic surgery, with meningitis in neurosurgery, with contamination of the cerebrospinal fluid as a result of spinal anesthesia, and with the contamination of tissues in local anesthesia, as well as with septicemia, gas gangrene, cases of tetanus, *etc.*, all this considered, as much as possible, without other factors of contamination (*loc cit*).

This list is worth consulting, for, although condensed here, it occupies about ten pages.

It represents the definitive and incontrovertible demonstration of the failure of the usual method, which was originally created in France by Terrier and which has been designated as aseptic, and we are thus made to realize to what extent an operation, under these circumstances, is a test of the power of the organism to resist infection, and how much it is to be desired not to submit the patient to this test.

Leriche, who has seen me operate and who has himself operated by my method at Rio de Janeiro, has appropriately said: "I have weighed all the theoretical objections which one can possibly raise against Guérin's method: difficulty, inconvenience, uselessness, expense. Not one of these is valid. We must not forget that in Lister's time, also, one did not believe that it was necessary to change anything in the traditional practice of surgery. All was well, because it was being done. How many terrible failures there were, nevertheless! And, more recently, have we not seen many surgeons declare themselves against the use of masks and gloves? Man, even if he is a surgeon, is an animal who succumbs to habit formation."

The third phase is total sterilization, the only procedure permitting integral asepsis, which has allowed me to demonstrate a type of healing previously unknown—Pasteurian cicatrization, which profoundly modifies the operative results and is the basis of the third phase of surgery.

THE EXOGENOUS FACTORS OF OPERATIVE CONTAMINATION

These elements are the patient's skin, the surgeon's hands, the patient's and surgeon's perspiration, the operative equipment, and the air.

The Skin of the Patient—The disinfection of the skin with tincture of iodine, which had been employed empirically for a long time, was studied

scientifically by Walther in 1909 (Bull et Mem de la Soc Nat de Chir , Congres Inter de Chir de Paris, 1910), by means of histologic sections which were impregnated with silver nitrate and which, through the formation of the iodide, made possible the observation that the iodine penetrates the entire thickness of the epidermis and the superficial layers of the dermis, the sebaceous and sweat glands, and the periphery of the hair follicles

However, when the time came to demonstrate by means of inoculations, that living bacteria were no longer present, the contamination of the air,

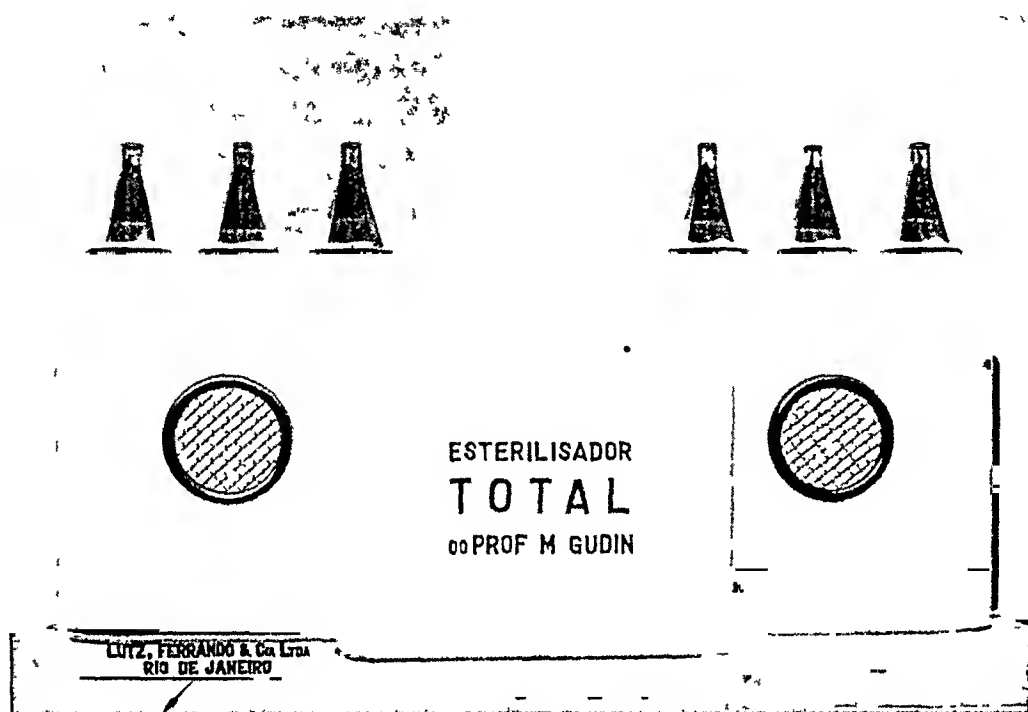


FIG 3—The Total Sterilizer One hour suffices for the sterilization of all the material required for several operations

inevitable with the ordinary bacteriologic methods, has vitiated the results, thus leaving room for doubt

The reason is that these experiments, like many others, are above the possibilities of present-day bacteriology, whether it is a matter of sampling of material for culture, or of inoculation, transfer, or tissue culture, or of any other bacteriologic technic, contamination by the air has always remained the stumbling block in bacteriology, an insurmountable one when certain demonstrations are attempted, for it has never been possible to work freely, in sterile air

The problem of the sterilization of the skin had not been solved, therefore, but has remained of the greatest surgical importance, and attempts had to be made to find an answer

This is why I have again undertaken these experiments, this time under the protection from contamination by air, and they have enabled me to arrive at the following conclusion The normal, healthy, accessible skin (the umbilicus is inaccessible, without anesthesia), without callosities, carefully

freed of fat by means of benzine, and treated for at least ten minutes with a freshly prepared 10 per cent solution of iodine, is and remains perfectly sterile

While one must be very careful to completely remove the tincture of iodine for culture experiments, it is quite unnecessary to do this for surgical operations if freshly prepared tincture is used

The Hands—The practical solution which alone permits to keep the skin of the hands in perfect condition consists, first of all, in avoiding their contamination, and subsequently in scrubbing them very carefully for at least ten minutes with hot water and sterile soap, without an antiseptic

In prolonging this procedure for more than a half hour, one can achieve a real sterilization of the hands, as has been shown by Delbet and Ravaut in 1904 (Bull Soc Nat de Chir)

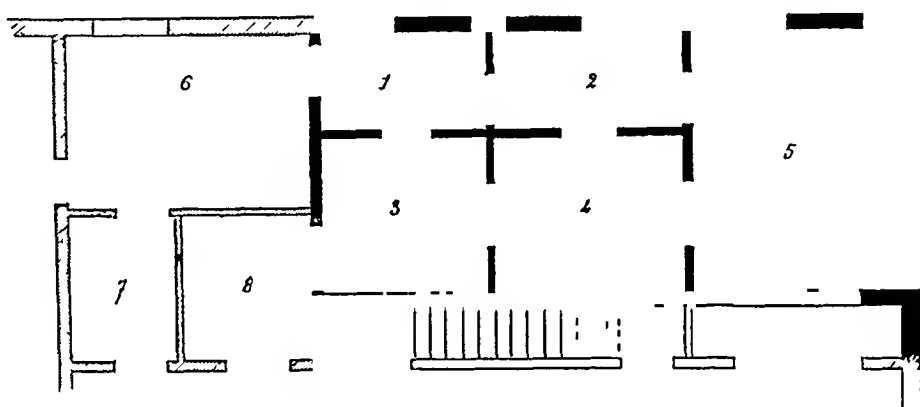


FIG 4—Plan of the lower floor of the operating unit with sterile air tight compartments of the two floor operating room 1 and 2—Surgeon's entrance 3 and 4—Patient's entrance 5—Operating room 6—Professor's room 7—Assistants' room 8—Room where the patient is undressed The portion which is indicated in black is that which is sterilized

They demonstrated at this time that the hands remained sterile when prepared in this manner and were covered by gloves, but that the latter were not sterile, because of their exposure to the air! But the hands do not resist a daily treatment of this sort In practice, as far as dressing and putting on gloves are concerned, one must proceed as if the hands were septic

Sweating—No asepsis is possible if the patient or the surgeon perspires In this connection, the use of conditioned air is imperative

The Operative Equipment—The sterilization of water, instruments, gloves, sponges, sutures, carried out according to a rigorous technic, taken by itself, leaves nothing to be desired

As far as catgut is concerned, this material is the source of numerous operative annoyances, as has already been pointed out by Kauffmann and Galea who studied the causes of postoperative tetanus (Jour de Chir, February, 1932) This source must be sought elsewhere Always sterile if it is transferred from sealed tubes into the culture broth in sterile air, as I have had occasion to observe in numerous trials, it produces cultures as soon as it is exposed to the air, just as any other surgical equipment It cannot be

doubted that by virtue of being wet it attracts a much larger number of bacteria than silk or linen threads, which are dry

As regards the question of postoperative tetanus in connection with operations without endogenous septic focus, the only surprising thing is the rarity of its occurrence, which must evidently be attributed to the fastidious requirements of an anaerobic organism like the bacillus of Nicolaier. The presence of tetanus bacilli in operating rooms is frequent. It is easy to see with what impunity operating rooms are soiled by dirt carried in on the



FIG 5—The surgeon completely protected by the sterile suit

shoes of assistants. It is not from the point of view of contamination that I consider catgut as an undesirable thread, while operating in a sterile medium, but because it is resorbable and therefore lacks solidity. Therefore I use it only exceptionally, namely, in septic cases or when other sutures would run the risk of undergoing a process of incrustation.

The Air in the Operating Rooms—The air is the source of contamination which it has not been possible to control. The construction of operating rooms with material which is easily washable, with rounded corners and a few other provisions, contribute very little to the battle against an element which is so subtle and mobile, and which surrounds us everywhere.

It consequently represents a permanent factor of contamination of the operative wound, unless it is sterile.

It acts (1) Through the bacteria which are suspended in the room air, (2) by the displacement of those which are deposited everywhere, (3) by the carriage of bacteria into the room by all persons, vehicles, and material coming from the outside, (4) as a carrier of bacteria from the respiratory pathways and mouth of those who talk, sneeze, and cough, even when they are protected by a mask, (5) under the influence of conditions of temperature, of currents, of the presence of water, which one finds in the form of vapor, drops of Flugge, microscopic droplets of Trillat (of the Institut Pasteur), which, because less than one micron in diameter, escape almost entirely the action of gravity, while containing "alimentary gases" which sustain life and reproduction of organisms. The latter are easily transported along great distances and without difficulty penetrate the pulmonary alveoli, in spite of the defensive apparatus of the respiratory tract, which is normally effective against bacteria which present themselves under different conditions (Trillat, C. R. de l'Acad. des Sci. Sur les Conditions de Transport des Microbes de l'Air, 1913, Influence de l'Humidité, 1920, Activité de l'In-

fection par les Voies Aériennes, 1921 and 1925, Influence des Agents Ex-
térieurs sur la Contagion, Rev d'Hygiène, June, 1932)

About 30 or more years ago, Miquel, Muller, Flugge, Lefoie, Fournier, Saitoy, and Tuffier studied the bacteria in operating rooms, more recent

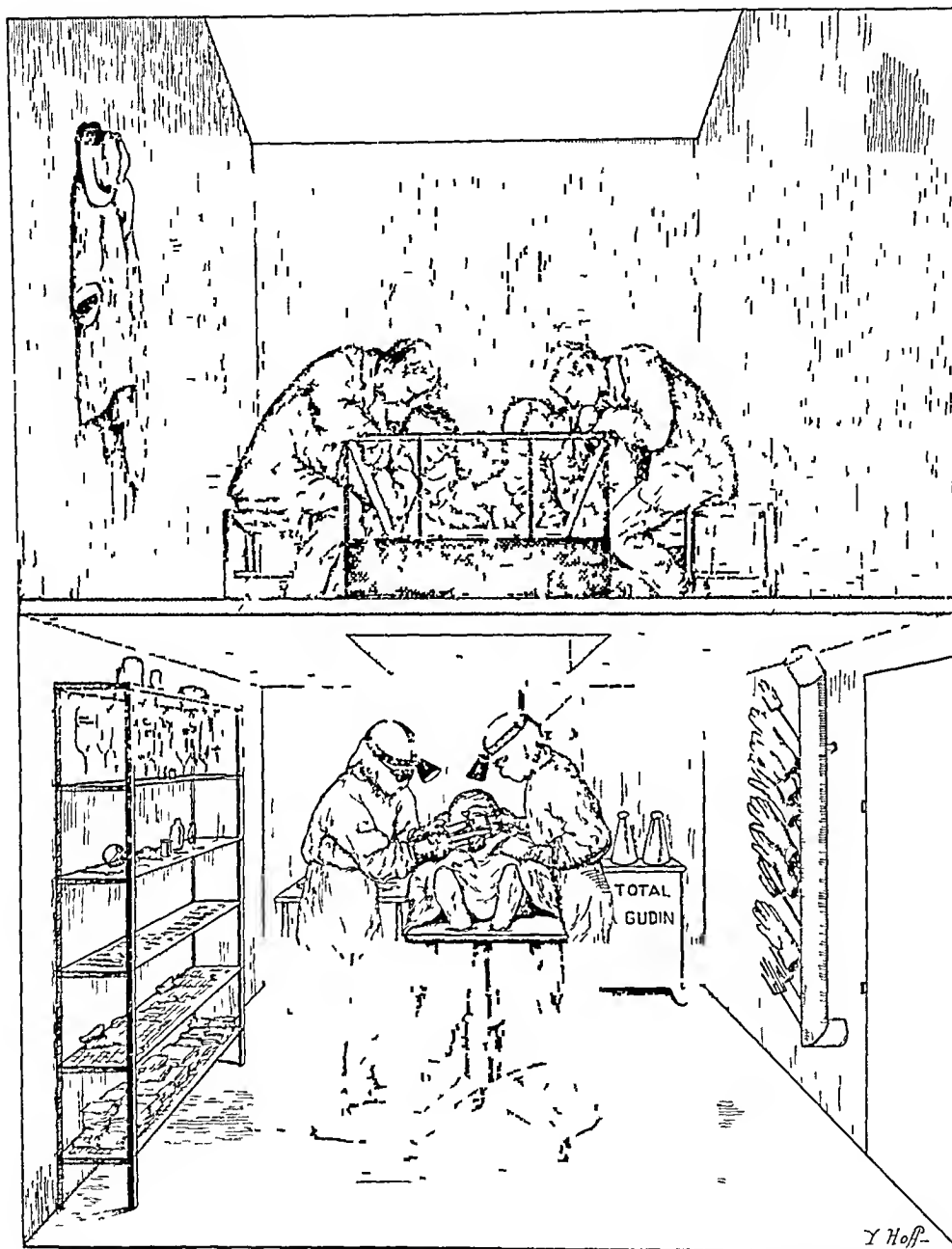


FIG 6—The operating room is very low, a very close view is obtainable directly down upon the operative field which fact enables one to see the operative details, so that the students really spend their time profitably

work has merely confirmed the data contributed by them. It was shown that the predominating pathogen is the staphylococcus, and others which were found are the streptococci, the colon bacillus, the pneumococcus, the tubercle bacillus, the tetanus bacillus, as well as other anaerobes, according to circumstances (Kole and Wassermann)

The most important work on this subject, however, which has since been confirmed by numerous authors, was that of Quemu and Landel (1902) who, after two years of much laborious research, published an important memoir in *Bull et Mem de la Soc de Chir de Paris*, under the title *Micro-organismes de l'Air dans les Salles d'Opérations Recherche d'un Procédé de Desinfection*

They have shown (1) That agar plates of a surface of 65 cm², exposed for an average duration of ten minutes, give an average of 80 colonies per plate, (2) that this number is tripled or quadrupled as soon as assistants, wearing sterilized gowns, enter the room, (3) that when a certain quantity of dust collected in the room is injected into guinea-pigs, abscesses, phlegmons, and septicemia are produced, in confirmation of the older experiments of Miquel, one of Pasteur's students, who during a period of 30 years had studied the problem of the atmospheric bacteria so well that very little has since then been added

Flugge, using *Micrococcus ferruginosus*, has shown that even when one speaks with a low voice, without a mask one contaminates agar plates at a distance of several meters

Numerous investigators have demonstrated with sufficient probability (considering that these experiments have a character of precision only in a sterile atmosphere) that even while wearing a mask the surgeon who talks contaminates plates at a distance

I have observed—and this observation is possible only in a sterile atmosphere—that the surgeon whose face is well covered and who breathes normally does not contaminate the atmosphere if he does not talk

The question of the contamination of the mask is a delicate one. The mask is always forcibly contaminated—first of all by the skin of the face if one forgets to sterilize it (as I have seen happen in the experiments which I know of), and, secondly, by contact with the mouth and the external nares, which regions cannot be sterilized

The local contamination of the mask is not necessarily followed by that of the atmosphere

The problem of the contamination of the air has been based on the conception of Lister who, at a time when the pyogenic bacteria were still unknown, was able to point out the analogies between the phenomena of infection and those of fermentation, which latter Pasteur had just demonstrated (1864)

Since the contamination of the air may be the result of various factors, and since further study results only in confusion the great majority of surgeons finally believed very little or not at all in atmospheric contamination

The statement made by Kauffmann and Gallea (*loc cit*) "Present-day sterilization and the use of gloves makes impossible the transfer of germs from the hands or the instruments of the surgeons," corresponds to the general conviction which, as I showed already in 1930 (Gudin *Presse Med*, April 16, 1940—*Methode Operatoire Sterile*), but is quite erroneous

THE REASON FOR THE FAILURE OF THE ATTEMPTS MADE TO
STERILIZE THE AIR OF OPERATING ROOMS

It is impossible to introduce a sterile substance into a container contaminated by bacteria without contamination of the substance

It is just as impossible to sterilize any substance in a container if the process of sterilization does not succeed in sterilizing container and content simultaneously

The disregard of these two fundamental bacteriologic facts is the reason for the failure of all attempts made to sterilize the air in operating rooms

In all these attempts one has never thought of using the means necessary for avoiding the contamination of the room, as Leriche has appropriately pointed out in his communication to the Royal College of Surgeons of London (April 5, 1939)

It is, therefore, useless to analyze and discuss in detail the numerous processes, all of which are vitiated by this fundamental error, such as filtration through various substances (Bellangei, Trenel, *etc*), the passage of the air through metallic gauze heated by electricity (Sartory), filtration through precipitation of dust by the action of high-tension currents (an American industrial Cottel process for the purification of smoke, proposed in France in 1938 for operating rooms by Pauthenier and Volkringer), the industrial process of "air washing" by means of antiseptic solutions (Gosset and others), the decantation of dust through a cloud of vapor (tried by Terrier a long time ago and recently vainly revived by Masmonteil in France), the hydrogen peroxide spray (Quénu, 1902), the formal treatment followed by the introduction of outside air (Flugge in Germany and Fourmer in France, 1904), the use of ultraviolet rays, *etc*, without even speaking of the initial process of Lister's carbolic acid spray (1865)

As regards the attempts at sterilization by means of water vapor under pressure, made in Italy a long time ago, it is superfluous to speak about them any further

Sterilization by means of ultraviolet rays, which at the present time still interests a few surgeons, has seriously occupied my attention since the beginning of my investigations. I mentioned this in my first paper on the subject, in 1930 (Gudin Presse Méd, April 15, 1930—Méthode Opératoire Sterile), saying "As a physical agent, ultraviolet rays suggest themselves automatically, but in their connection there still are problems to be solved in order to be able to sterilize perfectly not only the air—which is easy—but also the entire surgical environment"

Finally, after all sorts of hopes, I have arrived at the firm conviction that it is in no way possible to bring about total sterilization by means of ultraviolet rays, simply because, despite all possible "cross-firing," one does not succeed in sterilizing container as well as content, a *sine qua non*. This remains an incontrovertible fact

But ultraviolet rays, nevertheless, remain a valuable aid if—as I have done, in 1928, in the first operating room with water-tight sterilizable partitions which I built in the Gaffre-Guinle Hospital in Rio de Janeiro—one

places a series of ultraviolet lamps into the air-conditioning conduit, or if—as I am doing at the present time—one places the lamps into the air-conditioning apparatus, taking care, however, to absorb the liberated ozone by means of charcoal

INTEGRAL ASEPSIS

The method which I have conceived for avoiding exogenous operative contamination is based upon three fundamental factors (1) Obtaining a perfectly sterile operating room, containing all the surgical equipment, (2) employing all necessary means for avoiding the contamination of the air in this operating room and of the surgical equipment contained in the latter, (3) knowing how to execute the operation very precisely according to scientific bacteriologic principles

The first condition is realized by the process of sterilization which I invented in 1929 and which is based on the action of chemical agents—gaseous as well as in aqueous solution—through the medium of an apparatus (“the total sterilizer”) which is enclosed in a hermetically sealed operating room and electrically controlled from the outside, this apparatus can automatically maintain the conditions of temperature and humidity of the air in this room, without the introduction of outside air. This apparatus consists of several flasks containing the chemical substances, of a large pan containing a solution through which air is bubbled, and of special equipment for conditioning the air. The sterilizing agent is formaldehyde which is evaporated from a formalin solution, in amounts proportional to the size of the room, in an atmosphere saturated with moisture and vigorously agitated by powerful fans. It is obvious that no living being can enter the room which is thus saturated with this toxic agent. The latter must, therefore, be removed. This is done by the neutralization of the formaldehyde. Ammonia is evaporated in required amounts.

This substance combines with the formaldehyde in the air, and the atmosphere then contains hexamethylene-tetramine with an excess of ammonia and, therefore, does still not allow respiration.

For the removal of these chemicals from the air, the latter is bubbled through a solution of tartaric acid by means of a rotary compressor, and the air-conditioning apparatus is put into operation.

Hexamethylene-tetramine is soluble in the water, and the ammonia combines with the tartaric acid, forming ammonium tartarate, which is also soluble in water.

One thus obtains sterile air which can be freely breathed, a fact of paramount importance, on which rests the solution of the problem of integral asepsis.

Testing the Sterility of the Air—This requires a special technic, for it is impossible to introduce agar plates into the operating room from the outside because they are contaminated and would carry in bacteria, and furthermore the aspiration of a few liters of air does not provide a sufficient guaranty.

The following test has been made and repeated a number of times (1)

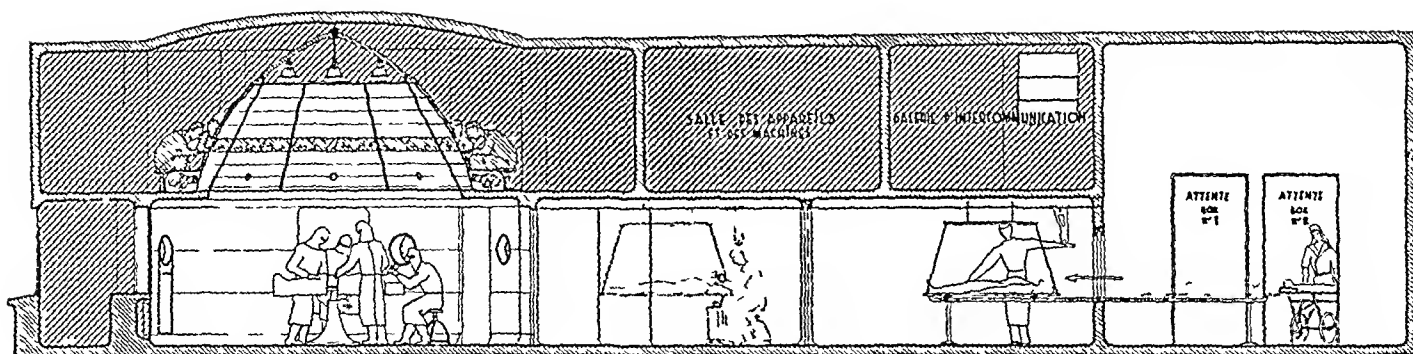


FIG 7—Reproduction of an internal view of the Gudrin sterile operating unit exhibited in actual dimensions, by the Surgical Academy of France at the Palace of Discovery at the International Exposition of Paris, in 1937 (*La Chirurgie* By Gosset, Fredet, and Monod, Masson & Co, publishers)

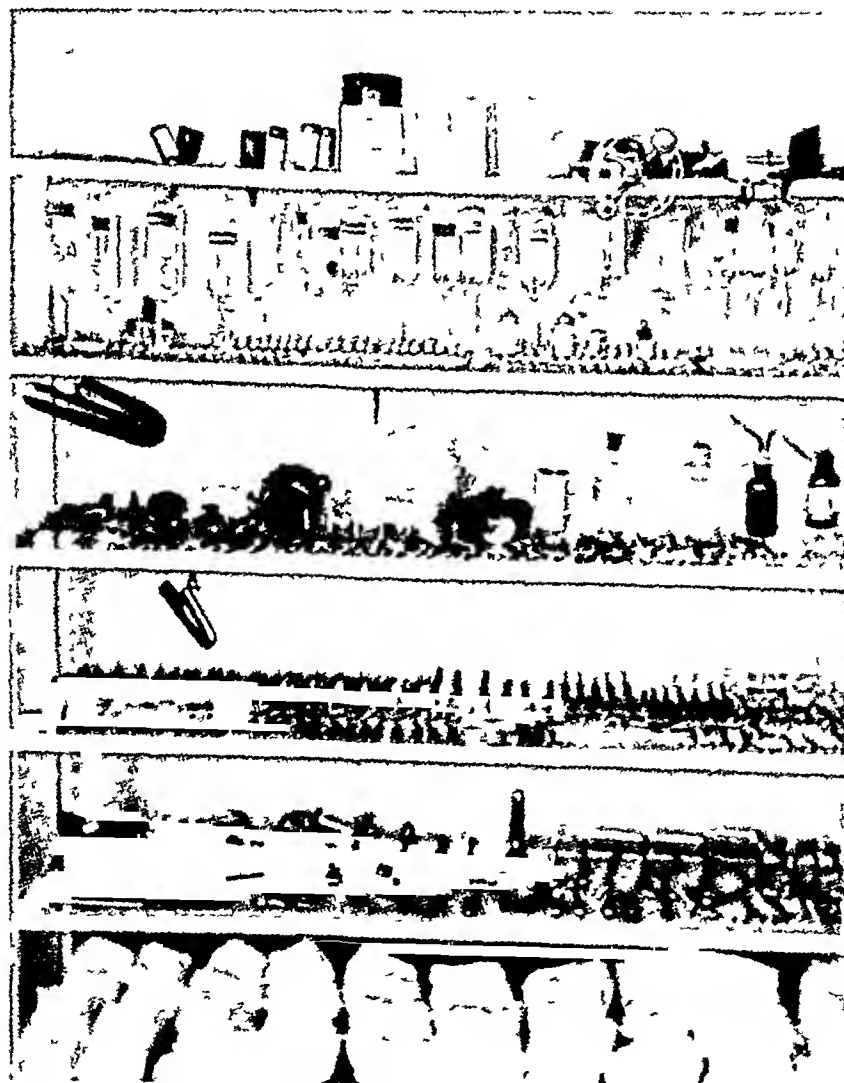


FIG 8—The chemical sterilization of the surgical equipment, the wire shelves

Agar plates are placed into the room, they are prepared in such a way that the gases do not come into contact with the agar. With this end in view, a small Petri dish containing agar is placed into a larger one not containing agar and is carefully surrounded with cotton. The whole is sterilized in the autoclave and is then placed into the room before the latter is sterilized. (2) After sterilization one enters the room, observing the precautions already described for avoiding contamination, and one opens the plates, which are then exposed for an hour or more to the powerful air currents produced by the fans. One thus circumvents the error which may arise from the existence of Trillat's droplets which, in principle, must disappear by virtue of the effect of the saturation with moisture and of the agitation of the air during sterilization. (3) The plates are now closed with the same precautions which were taken when they were opened. (4) Out of six plates, two are exposed to the outside air, in order to make sure that the formaldehyde has not penetrated and impregnated the agar. (5) Transfer to the incubator.

The result is always the same—four plates are sterile, and two are contaminated by the outside air.

The second condition. The operating room is isolated from the outside by four sterile anterooms—two for the preparation of the surgeons, and two for that of the patients—equipped with sterilizing air conditioners.

Surgeons and patients discard all their clothing before entering the sterile rooms. They are dressed in sterile overall gowns which cover the entire body, in the manner of diving-suits. The spectators are completely isolated.

The patient is brought into the room, already anesthetized, on a mobile operating table, to which the instrument trays and discard bags are attached, so that the entire unit can be evacuated as a whole to make room for the next patient.

Silence must be observed, for no mask resists if one speaks in a loud voice, or if one coughs or sneezes. No surgeons or assistants afflicted with upper respiratory infections are allowed into the room.

The hands are washed, in sterile air, with sterile hot water and sterile soap, with the aid of several successive sterile brushes, for ten minutes. Even under these conditions the hands are not sterile. The gloves remain sterile in a sterile atmosphere as long as they do not come in contact with a non-sterile object.

Sweating is prevented by conditioning the air.

The patient's skin is cleansed with benzene, and then treated for at least ten minutes with a freshly prepared 10 per cent iodine solution, which it is generally unnecessary to remove by means of alcohol.

After having resumed the study of the problem under conditions avoiding the sources of error which were inevitable with the ordinary bacteriologic methods, and having taken samples of skin, macerated them, and inoculated them into culture media in sterile air, I have arrived at the conclusion that the healthy, normal skin treated by this method is sterilized perfectly.

BRIEF COMMUNICATIONS AND CASE REPORTS

CALCIFIED INTRACEREBRAL HEMATOMA

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AND

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THE CASE herein reported is that of a large, solitary, spherical, calcified intracerebral hematoma. In a search of the literature, we were able to find only one similar case which had been verified by operation.

Levin¹ reported the removal of a calcified mass from the left temporo-parietal region which, when sectioned, showed "a laminated calcified mass, with traces of altered blood pigment, and an amorphous mass with calcifying spicules scattered in the substance. There is no evidence of tumours or of tuberculosis. The features are those of a calcified hematoma."

Case Report—F B, colored, male, age 46, was admitted to the Neurosurgical Service at the Louisville City Hospital, November 23, 1939, with the chief complaints of convulsions and pain in the right eye.

Present Illness—The patient stated that when he was 13 years old he jumped from a train, stumbled, and struck his head. He was unconscious for 15 or 20 minutes. He was kept in bed at home, but was not seen by a physician. He suffered from severe headache which lasted for several days. To his knowledge there was no nausea or vomiting at the time.

About one month after the injury he had his first convulsive attack. The attacks recurred at intervals varying from one or two months apart, to as long as three years between attacks. He began the use of luminal to control the attacks in 1917.

The patient described the attacks as all beginning with a sense of nervousness. He became "faintified" and learned to lie down immediately upon the occurrence of this symptom. He then had a peculiar feeling in the left leg followed by twitching and spasm of the left leg which then progressed to the left arm and left face. Later, he lost consciousness and was told that the right side of the body had become involved. After an attack the patient suffered from frontal headache for a short time.

Since 1935, he has complained of attacks of severe pain in the right eye which radiate back toward his right ear. This has been more severe recently.

Physical Examination—This revealed a well-developed, well-nourished, colored male, age 46, who was intelligent and cooperative. Weight 160 lbs, temperature 98.6° F, respiration 20, blood pressure 154/100. The general physical examination was negative except for the neurologic findings.

Neurologic Examination—This showed a complete left homonymous hemianopsia. The pupils were equal and reacted to light. There was no choking of the optic disks or other pathology in the eyeground examination. He had good motor power in all extremities. The superficial and deep reflexes were normal, and there were no pathologic reflexes.

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Laboratory Data—The urinalysis and blood count were within normal limits. The blood Kahn reaction was negative.

Roentgenologic Examination—Roentgenograms of the skull showed a dense, sharply defined, slightly irregular shadow in the right posterior parietal area, approximately midway between the vertex and base of the skull, and approximately midway between the right lateral wall of the skull and the midline. This shadow was approximately 4 cm in diameter and its general shape was spherical (Fig. 1).



FIG. 1.—Anteroposterior and right lateral views of the skull showing the calcified mass lying in the right occipital lobe. The shadow measured approximately four centimeters in diameter.

Operation—An osteoplastic flap was turned down in the right parieto-occipital area of the skull. The dura was under no tension and was opened along the posterior limb of the bone incision. The free edge of the dura was turned back to expose the cortex over the posterior portion of the parietal lobe and the anterior part of the occipital lobe. Inspection showed the cortex over the occipital lobe to be discolored in an area about 1 cm in diameter. This was a brownish discoloration instead of the normal grayish appearance of the brain. Palpation of the cortex revealed a hard mass in this area which seemed to be just beneath the cortex in the region of the discolored brain and, also, under the cortex of the adjacent parietal lobe for a distance of about 3 cm. A linear incision was planned parallel with the posterior limb of the bone incision to cross the discolored cortical tissue. Silver clips were placed on two cortical vessels and a 3 cm linear incision made in the cortex. At a depth of 1 cm the hard dense mass was encountered. This was found intimately adherent to the surrounding brain tissue. The brain substance was gradually dissected free from the mass by the use of cotton pledgets until the deepest portion of the mass was reached. At this point the ventricle was entered while attempting to separate the mass from the brain tissue, and it was found that the mass was intimately adherent to the wall of the ventricle with only 2 or 3 mm of tissue separating the ventricle from the mass itself. By removing a portion of the wall of the ventricle the mass was finally freed from the brain and lifted out of its bed. The opening into the ventricle was at the junction of the posterior horn and the atrium, and a good exposure was afforded of the entire lateral ventricle.

The choroid plexus was lifted up and a silver clip placed in the vessels leading to the glomus in order to decrease the production of cerebrospinal fluid

Pathologic Examination—*Gross* (Dr A J Miller) "The specimen is a spherical mass weighing 30 Gm. The color is dull-white and the consistency is that of stone. No vessels can be found entering the mass. The mass is sectioned with a saw. There is an outer hard shell 3 to 4 Mm. in thickness. The remaining inner portion is yellowish-brown in color and semisolid in consistency, suggesting necrotic blood."



FIG 2—Photomicrograph of periphery of calcified mass. The capsule is an old, dense, hyalinized connective tissue, and the interior is soft gummy material resembling a necrotic blood clot. Granules of calcareous salts are widely distributed in varying density. There is no leukocytic infiltration.

Microscopically, "the inner portion stains uniformly with eosin. There are numerous strands which are evidently partly broken down fibrin. Quite a number of forms that have the appearance of cells are noted but there is no differential staining and the outlines are not definite. The structure suggests a necrotic blood clot. Here and there are small diffuse deposits of calcium. The capsule is fibrillar but it also is uniformly stained with eosin. The fibrils are arranged parallel to the surface chiefly, and this entire outer zone is quite densely infiltrated with calcium salts. The structure suggests that organization of the mass was attempted but for some reason was arrested and necrosis and calcification followed. Clinging to the outer surface are a few small masses of brain tissue. These show some gliosis and pyknosis of the glial cells. There is nothing to suggest tumor growth." *Pathologic Diagnosis* "Hematoma, calcified."

Postoperative Course—The patient left the operating room in excellent condition. Blood pressure 140/96, pulse 90, respirations 20. He had conversed with the attendants during the entire operation. The second day after operation the patient began to show signs of increasing intracranial pressure. This was relieved by intravenous injections of 50 per cent sucrose three times daily. Later, several spinal punctures were performed to relieve headache. The patient was discharged from the hospital three weeks after operation. He was asked to report to the Out-Patient Department for medication to prevent the recurrence of any convulsions. Here, he was given a supply of Dilantin and instructed to take 3 gr. twice daily.

SUMMARY

Large, solitary, intracerebral hematomata are not a common complication of head trauma. However, they are frequent enough to justify consideration when the patient presents focal symptoms with increase of intracranial pressure following an injury to the head. In this clinic, six such intracerebral hemorrhages have been removed surgically. Presumably, many of the smaller ones are absorbed and the patient recovers without surgical intervention. For one to become completely calcified is certainly a rare occurrence.

In the case herein reported, the history indicates clearly that the hemorrhage into the occipital lobe resulted from head trauma 33 years prior to admission. The persistent severe headache immediately following the accident followed by focal convulsions one month later is in keeping with this assumption.

We do not expect that removal of the calcified mass will cure the convulsive episodes. We are hopeful, however, that the removal will facilitate treatment in much the same way that excision of a localized cortical scar facilitates the control of convulsions. The patient will be encouraged to continue an optimal level of sodium diphenyl hydantoinate therapy over a period of years.

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HEMORRHAGE INTO THE THYROID GLAND RESULTING FROM MUSCULAR EFFORT*

REPORT OF A CASE

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ALMOST ALL adenomatous goiters removed surgically show hemorrhagic areas as well as a fibrosis, and calcareous and hyaline degeneration. Such hemorrhages, however, are probably only of pathologic interest. Even the pathologist ignores them because his interest is more in the cellular and colloid changes which are primary and related to thyroid function. Hemorrhage into the thyroid, severe enough to cause symptoms, would not appear to be a common event. A fairly comprehensive review of the literature shows very few articles on the subject. McGregor and Cornett¹ claim it is a frequent occurrence, Ballin and Morse² comment on its frequency, yet Schwoerer,³ in a review of 2,500 thyroid operations, found only 18 cases of hemorrhage. Plummei,⁴ and later Plummei and Bioders,⁵ made a search for acute, painful enlargements of the thyroid at the Mayo Clinic and found only 16 cases. Of these, in only two was the enlargement so precipitous, reaching its maximum in a few minutes, that it was attributed to hemorrhage. At operation, marked hemorrhage was found. Clute⁶ states that while hemorrhage may occur in an adenoma of the thyroid it is rare. He reviewed his recent experiences at the Lahey Clinic in order to explain the alarming symptoms that sometimes occur in bad goiter cases. He cited two cases, and believes that during the last ten years they had had about six such cases.

In diagnosing the condition, malignancy must be ruled out. A good history is most important. In some cases, a tumor of the thyroid had been present for some time. In others, none had been noted. Then, on sudden physical exertion, which does not need to be necessarily heavy, pain in the neck and a sudden swelling occurred. This was usually followed by difficulty in swallowing. Abscess, though it has been reported, is even more unusual than hemorrhage.

Sometimes hemorrhage is so severe that coma and death ensue even in spite of operation. Wendel⁷ reports a case of rupture of the thyroid due to great hemorrhage in "a man, age 55, who, after straining at defecation, had sudden difficulty in swallowing, became unconscious, dyspneic and died in spite of emergency surgery to remove tension." McGregor and Cornett reported a case which also died. It was a spontaneous rupture of a cystic adenoma in a woman, the hemorrhage ruptured through the capsule and infiltrated the fascial and muscle planes of the neck spreading into the mediastinum. Von Ziemacki⁸ reports a somewhat similar case in a woman, with recovery. The blood extravasated anteriorly down to the level of the

* Presented before the Philadelphia Academy of Surgery, May 6, 1940

umbilicus. A number of other isolated cases are reported but with very meager details.

Case Report—B. C., white, male, age 45, a motor-truck driver. There was no previous history of any enlargement in the neck. He had had an appendectomy in

FIG 1

FIG 3

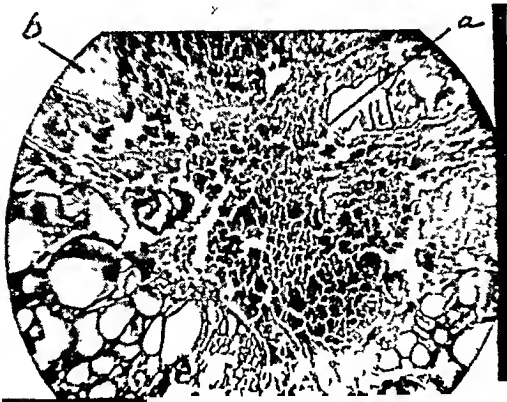


FIG 1—Shows massive hemorrhage, blood clots, blood pigment and serum in the stroma. In upper left, torn and isolated follicles in massive clot.^(a) Everywhere the hemorrhage has traversed the interlobular septa and rent them asunder. In upper right, organizing clot projects as a wedge toward center of section.^(b)



FIG 2

FIG 2—Shows colloid hyperplasia with giant follicle in upper center. Toward the left, there is a large blood vessel containing a massive clot.^(a) The walls of the vessel are not intact. Loose trabeculae of lobules appear infiltrated with hemorrhage which has separated the lobules. To the right of a giant follicle, there is hemorrhage extending downward. The blood has forced the loose tissue apart.

FIG 3—High power view of giant follicle showing colloid hyperplasia. In upper corner, there is one wall of large vessel in interlobular artery. Notice very thick fibrotic wall lined with endothelial cells and with fibroblasts and spindle cells in the wall. This vessel does not appear to be involved in the hemorrhage. Its arteriosclerotic and brittle walls have separated or receded from the lobule producing the gaping space noted.^(a)

childhood, and a fracture of the ankle about one year ago. He claimed to have always been in good health. His occupation always required moderately heavy lifting, and, occasionally, extremely heavy lifting. On August 2, 1938, while unloading bales from his truck "he felt something let go in his neck." He placed his hand there and noted a lump. His companion also noted it. He had no immediate pain but his neck felt uncomfortable and he had slight difficulty in swallowing. He was seen within a short time by his own physician and, later, was examined by another. The condition was more annoying than disabling. He stated that roentgenograms had also been taken of his neck. We first saw him August 30, 1938.

Physical Examination—The patient was a well-developed, well-nourished, muscular individual. The first thing noted was that, although he wore a tie, he was unable to button the collar of his shirt. Examination revealed an enlargement to the left of and just below the thyroid cartilage. It moved up and down on swallowing and was not adherent to the skin. It was not tender and no bruit could be heard over it. It was smooth and was about the size of a hen's egg. Pulse 80, blood pressure 125/75. The heart action was regular and of good volume, with no murmurs present. His BMR, however, was minus 14. **Clinical Diagnosis**—Hemorrhage into the thyroid gland or into a cystadenoma. Operation was not performed, however, until November 14, 1938—the

delay being due to whether or not this case could be considered as a compensable one. It was finally decided that it was.

Operation—Under avertin and 2 per cent novocain, a left lobectomy was performed. A cystic adenoma was found. The cyst contained clear, straw-colored fluid and old blood. The postoperative course was uncomplicated, and he was able to return to his work about six weeks following the operation.

Pathologic Examination—The specimen is the left lobe of a thyroid gland, with fibrotic capsule, measuring 8x5x4 cm. It contains a cyst over 3 cm in diameter near the outer or left border. The surface vessels are prominent and tortuous. On cut-surface, considerable colloid in very fine, pinhead-size, circular follicles can be seen. Between are areas of hemorrhage several millimeters to 2 or 3 cm in size. The cyst contains a clot, dark brown in color, 2 cm in diameter. It also contains straw-colored fluid. There is fibrosis and arteriosclerosis of the interstitial tissues. *Pathologic Diagnosis* (1) Interstitial hyperplasia of thyroid. (2) Massive hemorrhage into thyroid. (3) Massive hemorrhage into a cystadenoma of thyroid.

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ANOMALOUS DISTRIBUTION OF THE EXTRAHEPATIC BILIARY DUCTS

REPORT OF A CASE

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We wish to report an unusual anomaly of the extrahepatic biliary tract that was recently encountered. A search through the literature revealed one similar but slightly different condition.



FIG 1—Barium study of the stomach and duodenum showing the passage of the barium into the biliary ducts

Case Report—N Z, white, female, age 71, was admitted to City Hospital, January 9, 1940, complaining of abdominal pain. She gave a history of recurring attacks of indigestion for as long as she could remember, but two years before admission they became much more severe. There was no actual pain at this time, but rather a burning sensation in the epigastrium followed by bloating and belching, and later by nausea and vomiting. The attacks usually followed meals, particularly those containing fatty foods. She noticed jaundice on several occasions but never noticed clay-colored stools. Two weeks before admission she began to have severe epigastric and right upper quadrant pain with persistent nausea and vomiting. Icterus developed four days later, and had persisted to the time of admission. There had been a weight loss of 65 pounds in the last two years. There had been no other serious illness and no operations.

Physical Examination—The patient was a well-developed but poorly nourished white woman, appearing chronically ill. The skin was loose, inelastic and definitely icteric. The sclerae had an icteric tint. There were a few wheezing rales over both lung fields. The heart was essentially normal. The abdomen was pendulous, with tenderness in the right upper quadrant, and the sensation of a mass in that region. Pelvic and rectal examination gave no additional information. Red blood count 4,250,000, with 85 per cent hemoglobin, 17,400 W B C. The urine showed traces of bile and an occasional pus cell. The stools were all dark brown or green. Blood urea nitrogen 85 mg, icteric index 21, blood cholesterol 250. The Kline test was negative.

Röntgenologic Examination—Studies of the gallbladder and upper gastro-intestinal tract (Figs 1 and 2) showed several small shadows in the region of the duodenal cap,

which seemed to be due to the passage of barium into the biliary passages. The gallbladder did not visualize. There was slight spasm of the pylorus but otherwise the stomach and duodenum appeared normal. A plain roentgenogram of the abdomen showed no definite evidence of an abnormal soft tissue mass or of calculi. A roentgenogram of the chest showed the heart to be slightly enlarged.

Several diagnoses were suggested in view of the peculiar roentgenographic findings: (1) Cholecystoduodenal fistula from ulceration of a biliary stone, (2) carcinoma of the ampulla or of the head of the pancreas, and (3) chronic cholecystitis with cholelithiasis.

Operation—Celiotomy. The gallbladder could not be found. The common duct was dilated but no stones were palpated, the duct was not opened. The stomach and duodenum appeared normal. The abdomen was closed without further procedure. The patient did not tolerate the operation well, and the course was complicated by dehiscence of the wound on the fifth postoperative day, and evisceration. She died on the fourteenth postoperative day.

Autopsy—The liver was found to be essentially normal. A single hepatic duct emerged from each of the two lateral lobes. These joined immediately, to form a single main hepatic duct which was greatly dilated, obtaining a maximum circumference of 31 mm. Four centimeters from the hilum of the liver this duct divided into two branches. One branch emptied into the second portion of the duodenum at the ampulla of Vater, in common with the main pancreatic duct. The other branch emptied into the posterosuperior aspect of the lesser curvature of the stomach, 1 cm proximal to the pyloric ring. Microscopic examination at various points showed the wall to be characteristic of the extrahepatic biliary duct system, except for the distal 2.5 cm. At this point gradual transition to gastric wall occurred. No evidence of a gallbladder was found.



FIG 2—Oblique view showing the biliary ducts outlined by barium. In retrospect, this view shows two branches of the common duct, the one emptying into the stomach and the other into the duodenum.

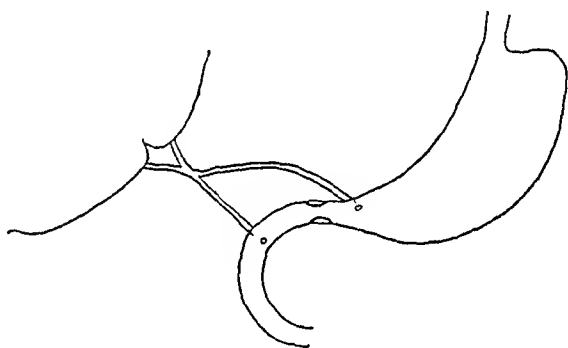


Fig 3

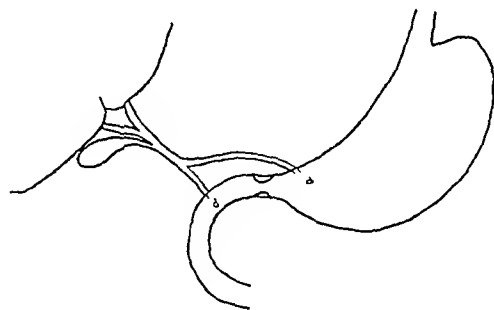


Fig 4

FIG 3—Our case showing congenital aplasia of the gallbladder and high bifurcation of the common duct, one branch emptying into the second part of the duodenum, the other branch emptying into the stomach near the pylorus.

FIG 4—Vesale's case, similar to ours except for the presence of the gallbladder.

COMMENT—We have been able to find only four other cases, in the literature, in which the common duct emptied into the stomach. Laennec

and Bleifuss have each reported one such case¹ According to Owen,² this is the normal site of bile drainage in the bream, an European fresh water fish Filippini described a case in which the common duct emptied into the stomach through the pylorus³ Vesale reported a case in which the common duct bifurcated, the upper duct emptying into the stomach above the pylorus, the lower duct emptying into the duodenum However, the gallbladder was present in this case (Fig 3)

Aplasia of the gallbladder has occurred three time in a series of over 13,000 autopsies recorded at City Hospital There were no other anomalies of the common duct found in this series

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NYLON SUTURE *

DERMONT W MELICK, M D

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THE POSSIBILITY of using Nylon as a surgical suture suggested itself when, in 1938, it was learned the DuPont Company had developed a synthetic substitute for silk. In view of the fact that many surgeons are advocates of silk it was thought Nylon might find equal favor should it have the qualities attributed to silk.

Physical Characteristics—The physical characteristics of Nylon¹ as compared to silk are shown in Table I.

TABLE I
PHYSICAL CHARACTERISTICS OF NYLON AS COMPARED TO SILK

	<i>Nylon</i>	<i>Silk</i>
Relative tensile strength	1 3%	1 0%
Elongation	25 7%	12 9%
Loss in strength when wet	14 7%	24 5%
Approximate moisture content under standard conditions	3 0%	15 0%
Elastic recovery under controlled conditions	77 0%	65 0%

The Nylon suture may be obtained† either as a single strand suture, called monofilament, or a multiple strand suture, called multifilament. The multifilament looks and feels very much like silk. The monofilament is comparable to the commonly known “dermal” and “tension” suture.

Animal (dog) experimentation was resorted to in order to study the effect of various sutures (catgut and silk as well as Nylon) in relation to tissue reaction and to the process of wound healing as ascertained by gross and microscopic studies. Nylon monofilament, Nylon multifilament, silk, plain and chromic catgut were imbedded in the anterior abdominal wall of dogs, and, at intervals between two days and 103 days, biopsies were taken and paraffin sections made. Intestinal anastomoses were also performed for comparison between fine chromic catgut (No 00000) and Nylon multifilament (No 000).

Results—The results obtained are graphically illustrated in Chart 1.

Clinical Use of Nylon Suture—Following experimentation on animals it was thought Nylon multifilament was worthy of a trial in the human. It was used as a suture on a limited number (ten) of hospital patients, in the performance of inguinal herniorrhaphy only. Five different operators used the suture in order to obtain individual reactions regarding its good or bad points. The opinions voiced were favorable. It was agreed that the suture was comparable to silk in the way it handled. The greater tensile strength of the suture as compared with silk of a similar size was particularly noted by each operator.

* Abbreviated report of a thesis presented to the faculty of the Graduate School of Medicine, University of Pennsylvania, in partial fulfillment of the requirements for the degree of M Sc (Med) for graduate work in surgery.

† All Nylon sutures for this study were supplied by Bauer and Black, Chicago, Illinois, through the courtesy of Mr Paul F Ziegler, Director of Curity Research Laboratory.

Wound healing was satisfactory in all of the patients upon whom Nylon multifilament was used as a suture. The incisions presented a minimal amount of reaction. The deep fascia and subcutaneous tissue was free of the diffuse induration noted with catgut suture.

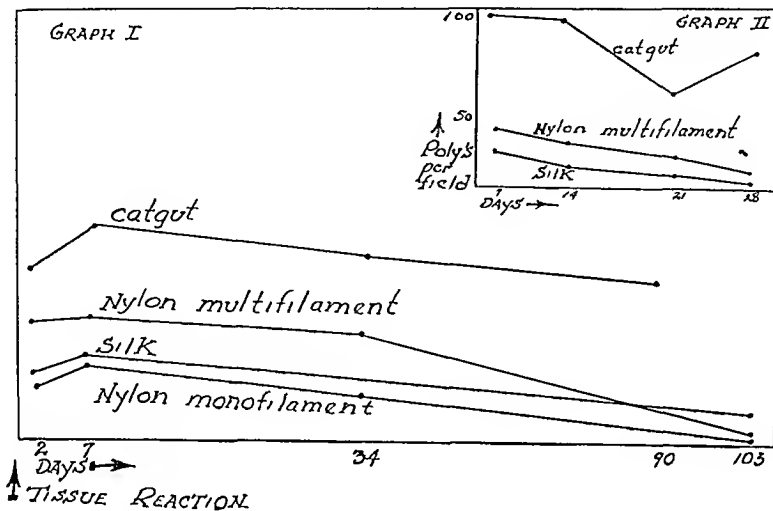


CHART I

Graph 1 illustrates the relative reaction of the tissues to the different sutures studied. Catgut caused the most tissue reaction and Nylon monofilament the least tissue reaction.

Graph 2 (inset) is adapted from the findings of Nichols and Diack.¹ They measured the tissue reaction to suture material by the number of polymorphonuclear leukocytes found per high power field.

SUMMARY—(1) Nylon multifilament causes less reaction in the tissues (of dogs) than does catgut. In the earlier stages of healing Nylon multifilament causes more reaction than does silk. The end-result of the healing process is practically the same for both Nylon multifilament and silk.

(2) Nylon multifilament is not completely noncapillary. Monocytes were heavily infiltrated between the interstices of the suture, when examined at the end of 34 days.

(3) Nylon multifilament is superior to silk in that it has a better tensile strength for comparable sizes.

(4) Nylon monofilament causes less tissue reaction than any of the sutures studied. It is not so flexible as Nylon multifilament, is more difficult to handle, and has a tendency to slip when tied with the usual surgical knot.

CONCLUSION

Nylon multifilament may be recommended as a satisfactory surgical suture.

Experimental and clinical studies were carried out under the supervision of Dr. E. R. Schmidt, Professor of Surgery, University of Wisconsin School of Medicine, Madison, Wis.

NOTE—Since completion of the above report fifteen additional herniorrhaphies have been performed using Nylon multifilament No. 0 as the suture material. Tissue reaction has been minimal and wound healing satisfactory in all cases.

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INTRA-ABDOMINAL RUPTURE OF RETROPERITONEAL TUBERCULOUS LYMPH NODE

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UNUSUAL clinical, operative, and pathologic findings in a patient who presented signs of an acute abdominal catastrophe is the occasion for the appended report

Case Report—R. S., white, male, age 21, was admitted to the Lakeside Hospital, stating that he had been awakened at about 6 A.M. (four hours previously) by an extremely severe, burning epigastric pain. The flexed position into which it forced him made it difficult for him to get out of bed. He became nauseated but did not vomit. Although there had been no change from the regular bowel habits, two cathartic pills were taken upon the advice of his parents. The severe pain continued and difficulty developed in breathing.

The previous history was negative except for epigastric pain for two to three hours after each meal, which was first experienced about a week before the present episode. However, this had not prevented him from eating many handfuls of peanuts on the previous day. He had felt entirely well otherwise except for a common cold of moderate severity. Abdominal examination showed board-like rigidity especially in the epigastrium. Despite the recency of the onset the temperature was 101° F (38.2° C). White cell count 20,000.

Physical Examination—The patient was well-developed and well-nourished, he lay very quietly in bed as if afraid to move. His face was flushed, the respirations were rather shallow and at 28 per minute. Grunting sounds were absent and there was neither cough nor movements of the alae nasi. Severe suffering was obvious. The abdominal pain, though general, was localized by the patient as most intense in the umbilical region. The abdominal wall was splinted, and the board-like rigidity extended to the midhypogastrium, beyond which it was slightly but definitely less resistant. Maximal tenderness was also located in the region of the umbilicus. Rectal examination was negative except for moderate tenderness everywhere to high fingertip pressure.

The temperature had risen from 101° F (38.2° C) to 103° F (39.4° C) during the past two hours, the pulse rate had increased to 110 per minute. The second white cell count showed 16,000. The urine contained a slight trace of albumin, and an occasional white cell in the centrifuged specimen.

Except for evidence of moderate nasopharyngitis, the remainder of the examination was negative. As pneumonia was considered, particular attention was paid to the lungs by two observers. A roentgenogram of the subdiaphragmatic region indicated the absence of free gas in the abdominal cavity.

Evidence adequate for a diagnosis of acute peritonitis was obvious but a likely explanation for the rapid and relatively marked rise in temperature was not apparent. Neither could the height of the leukocyte count be satisfactorily correlated with a diagnosis ordinarily associated with such rapid onset, the obvious severity of the pain, and the distribution and degree of abdominal wall spasticity.

Operation—Under general anesthesia, the peritoneal cavity was entered through a low upper right paramedian incision. A small amount of thin, turbid fluid was encountered. A culture of this was made. The appendiceal region was first inspected and a considerable amount of fluid was aspirated. No abnormality was found. The serosa was normal in appearance and, except for the fluid, no evidence of inflammation was found until the intestines were packed away from the upper abdominal structures. A few fibrin deposits were encountered on the anterior aspect of the pylorus, but the

distal end of the body of the stomach and duodenum as well as the gallbladder appeared normal. High along the edge of, but quite indistinguishable from, the gastric wall along its lesser curvature there was exposed a roughly oval, red-brown surface, approximately 6x6 cm in size. At the upper end of this there slowly exuded about 2 cc of thick white material from a slightly raised, deep blue conical eminence, 2 to 3 cm in diameter. Slight pressure in exploration expressed 3 or 4 cc more. This was removed with moist gauze and a crater-like depression surrounded by firm indurated tissue was palpated.

The inspissated material, the crater, the firm induration, and the red-brown color of old extravasated blood, which was evident in the surface layer, clearly indicated a relatively indolent process. These underlying tissue changes obviously antedated the onset of the patient's acute symptoms and probably the subacute as well.

Three mattress sutures were placed for infolding, but as the tissue was bound down and too unyielding, a flap of the great omentum was brought up over the region of the pathologic process. This maneuver, dictated by the circumstances, coincided with the advice of Braithwaite.² The flap was held in place by snugly tying the lower two sutures over it and by including its distal edge in the highest suture. The wound was closed without drainage.

Postoperative Course—All signs of peritonitis disappeared, but clinical and roentgenologic evidence of a widespread pneumonitis developed. The patient died on the third day.

Autopsy—Limited to the abdomen and chest. Performed at the Institute of Pathology by Drs. C. C. Couch and E. S. Ingraham, Jr. Dr. Howard Karsner kindly reviewed the material. There was widespread, confluent bronchopneumonia. There was no evidence of general peritonitis. Caseous tuberculous and calcified lymph nodes of the celiac group were found. The center of one of the nodes in the gastrohepatic ligament was partially liquefied, and one wall of it had been replaced by omentum firmly attached (that placed at operation). Formalin introduced into the esophagus was made to distend the stomach and duodenum, without leakage at any point. Careful examination of the gastric and duodenal mucosa and of the mesenteric nodes of the small and large bowel showed no abnormality.

The liver and spleen contained several hard yellow nodules 1 to 3 mm in diameter, which were probably, but not proven to be tuberculous.

Histologic Examination—The celiac nodes were demonstrated to be almost entirely replaced by large and small nodules composed of broad fibrous borders, surrounding granular and frequently basophilic amorphous centers. In the open node (covered by omentum), an unusually large caseous center was present, together with a small amount of fresh granulation tissue, heavily infiltrated with lymphocytes, plasma cells, and a few polymorphonuclear leukocytes. In this region, were several small active tubercles composed of young endothelioid cells, a few contained small necrotic centers. Associated with the tubercles were several giant cells of the Langhans' type.

The adjacent serous surfaces showed a thin layer of fibrin enmeshing moderate numbers of lymphocytes and granulocytes. In some situations there was early organization of this exudate. Examination of the gastro-intestinal tract was negative, and sections of the bowel remote from the pylorus showed a thin, normal serosa. Culture of the peritoneal fluid resulted in no growth after six days.

Review of the roentgenograms of the upper abdomen showed several large calcified nodes in the central portion. In the region of the spleen, there were numerous shadows of the density of calcium, about 3x3 mm in size, which, probably, represented calcified tuberculous foci in that organ (Fig. 1).

COMMENT—Among the large number of cases of abdominal tuberculous lymphadenopathy reported in the literature, the descriptions of a few cases of ruptured lymph nodes were found. Iselm⁶ reported six, Newboldt⁷ reported

two, Colt and Clark¹ one, Head⁵ one, and four cases were referred to in Anderson's¹ series

The outstanding findings in the case presented herewith were Preoperatively, extreme pain of rapid onset, abdominal wall rigidity, an early and extensive rise in fever, and a high leukocytosis. At operation, minimal evidence of general peritonitis which was limited to a moderate amount of free serous



Fig. 1.—Roentgenogram showing multiple areas of increased density in the region of the spleen and in the central portion of the upper abdomen

fluid, and the regional deposits of a few flakes of fibrin, visceral peritoneum of normal appearance save in the lesser omentum about the ruptured abscess. Postoperatively, disappearance of signs of peritonitis, and only slight and local evidence of such at autopsy.

In interpretation, the discomfort during the week prior to the acute episode was correlated with the regional inflammation about the retroperitoneal tuberculous lymph node abscess. In two cases of rather large retroperitoneal tuberculous lymph node masses, described by Ravdin,⁸ pain was not a prominent complaint.

The board-like abdominal rigidity and the extreme pain, best described as agony, indicated the presence of a substance in the released contents of the tuberculous abscess which was extremely irritant to the parietal peritoneum. In a case of ruptured tuberculous lymph nodes in the ileocecal region, reported by Head, the peritoneal irritation was evidently comparably intense, as the pain was sufficient to cause the patient, a young adult male, to "double up and roll on the floor." Rigidity in the abdominal wall was also found.

The early advance in fever was consistent with the observation of Fraser⁴ that "fever introduces the illness in cases of acute tuberculous lymphadenitis", also, with that of Braithwaite who considered a fever over 100° F (38.0° C) as suggestive of this disease rather than of appendicitis.

Rupture of the tuberculous abscess of the celiac group of nodes into the upper abdominal cavity resulted in a process which was, evidently, an unusual type of acute nonpyogenic, or of an aseptic peritonitis. The process was notable, not only for the evident intensity of the stimulation of the sensory elements of the parietal peritoneum but, also, for its prompt and marked general systemic effect. The unusual combination of considerable early fever and very severe abdominal pain, with rigidity, may serve as clarifying evidence in the preoperative diagnosis in the rare case of free rupture of a tuberculous abscess into the general peritoneal cavity.

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MEMORIAL COLLECTION FOR DR. JOHN B. DEAVER

The Lankenau Hospital, Philadelphia, Pa., is collecting material concerning Dr. John B. Deaver for a Memorial Collection in its library.

Photographs, letters, memorabilia, reviews, press comments, articles by or about Dr. Deaver will be greatly welcomed and appreciated. Photostatic copies can be made of material available for loan only. All communications should be addressed to the Library Committee, The Lankenau Hospital, Philadelphia, Penna.

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MEETING HELD AT PINEHURST, N C

DECEMBER 9, 10, 11, 1941

ADDRESS OF THE PRESIDENT

"ONCE AGAIN"

HARRY HYLAND KERR, M D , C M

WASHINGTON, D C

TWENTY-THREE YEARS AGO, in 1917, the thirtieth meeting of the Southern Surgical Association was held in St Augustine, Fla., under the brilliant leadership of the late Dr William D Haggard. In his Presidential Address, Doctor Haggard, with his great gift of oratory, called the Medical Profession and the Southern Surgical Association to arms in the First World War that he glowingly described as one of the "most magnificent events in all history." With what stirring words he pictured the glorious part our country was taking in that historic event—with no selfish ambitions of territory or power, we were hurling our mighty strength on the side of Democracy. He paid a glowing tribute to our World War President, whom he described as "that glorious seer, that incomparable patriot, and immortal statesman, Woodrow Wilson, Prime Minister of the World."

Doctor Haggard painted with eloquent words the exalted rôle the United States was to play in the future of the world. He said "The pages on which the history of this most holy of wars will yet be written will be illuminated with the great white light of our pure and sustained desire to benefit the cause of humanity." "If our nation lives up to its plighted word it will gain for itself new honor and imperishable fame."

In the World War the United States trained, equipped, and sent overseas an army of 2,000,000 men to throw the balance of power in favor of the Allies,

* Presented before the Southern Surgical Association, Pinehurst, N C, December 9-11, 1941

and bring the carnage to an end. Then the United States, through its President, who personally attended the Peace Conference, practically forced an agreement among nations for mutual protection and mutual benefits—the League of Nations.

It seemed at that time that, indeed, we had made the world safe for Democracy, and we had fought the last great war to end wars.

But selfish and myopic interests arose in this country to defeat the plans of peace. The League of Nations was emasculated by our refusal to assume our proper place at the Conference Table. The plan was doomed to failure because the United States, the only solvent nation on earth, basely turned its back on the very League of Nations that it had forced upon the Peace Conference. We were the great creditor nation of the world. The other nations had been bled white of their most precious blood and all their liquid capital. They were devastated economically. They all owed us huge sums of money that they had borrowed to stem the advance of autocracy. They could not pay in cash, and we made it impossible for them to pay in kind.

We raised insurmountable tariff barriers so that the product of their labor could not be sold in this country. The natural place we should have assumed in the vanguard of the rehabilitation and reconstruction of war-torn Europe was but a gesture. True, we later advanced further huge sums, not only to our late Allies, but to Germany, smarting under her defeat and weighted down with unpayable reparations. What part of this money went indirectly for preparation for the present war is uncertain.

It was only natural that Europe, stewing in its poverty, should fall victim to the demagogue. He raised their hopes of salvation, he put them to work, and then organized them for war. His very success at the beginning begat a need for more success. He cast his eyes abroad for those natural resources that his own country lacked. He began a campaign of expansion. When this had been accomplished by treachery, lying, and perfidious practices, when one defenseless nation after another had been crushed under the tyrant's heel, the world was again faced by the same problem as in 1914. All the liberties and all the freedom that man had struggled for since the Renaissance were again threatened. From the muck of devastation of the World War arose this monster bent on supreme domination of the world, and on placing the German nation in command, and all other nations in vassalage.

From the perspective of nearly a quarter of a century, we can now look back on those stirring times with critical eyes. The world again is in the throes of a mighty holocaust of war, again, autocracy raises its selfish might to rob the human race of all its hard-won liberties, again, the freedom of the individual is threatened, and again we answer the call of our brother man and advance to his aid.

Can we not gain some knowledge by studying our successes and failures of that time?

To the Medical World of our country, war came, in 1917, as an unforeseen, unpredicted and unprepared-for calamity. To the credit of our then

Surgeon-General, William C. Goigas, be it said that the tremendous task of organizing the Medical Corps of the Army was brilliantly and successfully accomplished. Our boys were well taken care of. The records of the Medical Corps compare favorably with the accomplishments of all other combatants. No soldiers in all history have been better treated.

The record of the evacuation service, of the evacuation hospitals, and of the base hospitals in France is a magnificent one. The medical profession had responded nobly to the call, and those who had been assigned duty with the A E F acquitted themselves splendidly. Unfortunately, when the need was greatest for medical men overseas, there were several thousand medical officers undergoing military training at Fort Oglethorpe, Ga. Surely, it is not necessary for the army surgeon to learn to drill unless he is assigned to troops. At the Medical Field Service School facilities have been established to train 500 student officers every two months. Refresher courses in administration and special professional courses for reserve officers are given in the permanent general hospitals.

Though the medical men of the A E F did a good job, we can now see how that job could be improved. As the principal function of the medical corps is to maintain the fighting strength, our greatest responsibility is to get the wounded back to their commands as soon as possible. This means rapid and smooth evacuation after proper triage.

As Lyle and Darrach have pointed out, the best interest of the fighting force is served if the effort in the forward area is concentrated on treating the lightly wounded. A superficial wound, properly treated within a few hours, may heal promptly and the soldier soon returned to his outfit. When the effort at the front is concentrated on the seriously wounded, the lightly wounded wait their turn in times of stress, and frequently become so seriously infected that a minor wound becomes a major one. In these forward Evacuation Hospitals capable surgeons, using three or four operating tables each, can turn over 80 to 100 lightly wounded cases in a 12-hour shift.

The use of the new sulfa drugs and their applicability to battle casualties will, no doubt, be an interesting and important development. The first aid kit of every soldier now contains a quantity of sulfapyridine.

The seriously wounded and the so-called nontransportable cases should be evacuated as soon as shock is controlled and the simplest of immediate procedures carried out, such as closing sucking wounds of the chest, preventing possible evisceration, and controlling hemorrhage. To this end special teams are invaluable. Shock teams, transfusion teams, splint teams, *etc.*, amply proved their worth in France.

Evacuation by airplane for the seriously wounded, if practicable at the scene of action, would be ideal for this type of case.

It is evident from the experience of the A E F that major surgical procedures should not be performed in the area of advance. Though it is hazardous to move certain seriously wounded cases, the final results will be better if their surgical treatment can be carried out in a well-equipped, stable base.

hospital Here specialization can be employed to greatest advantage All the modern and sometimes elaborate equipment for particular types of surgery will be available And, here again, all the modern developments in postoperative care will be at hand

Not only were the sick and wounded of the A E F efficiently cared for, but the boys at home got excellent care The influenza epidemic was devastating, and the mortality high, but the experience of the Army in this catastrophe led to real contributions to our knowledge in the handling of this disease, and particularly the handling of a common complication—empyema

When the casualties were discharged after the war, a huge bureau of the government was established to take care of them Their economic as well as their physical welfare was looked after Medically, the discharged soldier of the U S Army has been spoiled to a degree Not only disabilities incurred in action, but also disease acquired since discharge, are now being treated by the vast Veterans' Administration, with its 91 hospitals and 80,000 beds

The continued payment of total or partial disabilities to the soldiers has developed a functional element engrafted on their organic disease that can never be eliminated Thus we are not only paying our wounded soldiers large sums on account of their honorably acquired wounds, but additional large sums for purely neurotic and hysterical manifestations

At the present time this government has spent \$20,000,000,000 on its World War soldiers The cost *per annum* is now \$900,000,000, plus The Veterans' Administration predicts this sum will increase until 1951, when they will have 100,000 beds

The largest sum on this bill for medical cost of the World War is the care and hospitalization of the neuropsychiatric patient There are now 35,000 such patients receiving total, permanent disabilities The cost per neuropsychiatric case is from \$33,000 to \$38,000 per man

How can this huge item of the cost of the war be lessened? By weeding out the men with unstable nervous systems in the first selection

As the late Dr Thomas Salmon, formerly Consultant in Neuropsychiatry, A E F, said "It is only the doctor of the Local Draft Board who is able to cull from the selectees the man with the abnormal nervous system" The local doctor may know the registrant or his family and recognize from the registrant's personality or his background that he is nervously unfit for military service

The man with the perfect physique, but with the unstable nervous system, may go through the war without a scratch, and yet become totally disabled when he "cracks" on going into action He will be paid total and permanent disability for the rest of his life Had his mental instability been recognized on his selection, and had he been kept out of a combat unit, he could have served his country and been discharged a healthy individual, to assume his normal place in the community

The present draft law does not take this lesson sufficiently to heart There was no specific provision made for psychiatric examinations However, on

November 7, 1940, the Selective Service issued Medical Circular No. 1, at the insistence of the White Psychiatric Foundation. This circular stressed the importance of referring draftees of questionable personality to a psychiatrist before induction. The average doctor on the Draft Board might have made no attempt whatever to discover the type of individual he was examining. A brief questioning may give the clue for a more exhaustive examination that will save the boy's future happiness and his country's wealth.

The result of a year's experience in the present Selective Draft is alarming. Nearly 50 per cent of the boys have been turned down because they are physically unfit—truly an amazing figure. But of those rejected only 6.3 per cent were refused for psychiatric causes. In the World War only 33 per cent were rejected, and of those only 4.5 per cent on psychiatric grounds.

The selection of draftees is soon to be taken out of the hands of the Selective Service Boards and turned over to the Army. This change is fraught with great danger. There is grave question whether the Army can eliminate the potential neuropsychiatric case as well as can the physician of his local Draft Board.

In the modern army close order drill has been entirely done away with. The soldier is more than ever an individual. He has not the support and comfort of close companions. He must more or less fight alone. He needs more than ever a stable, well-balanced nervous system. Again, modern armies are to a great extent mechanized. The soldier must have sufficient intelligence to handle sometimes complicated machinery. The responsibility of the modern soldier is much greater than his predecessor—much more depends on him as an individual in a modern army than ever before. Should he fail under fire the consequences are far greater to his command than with the soldier of the last war. He must be physically fit, with a well-balanced nervous system, and, finally, thoroughly trained. It is simple enough to pick out of 130,000,000 people as many physically fit young men as we need, but to be sure they are mentally and nervously sound is a much more difficult problem. Through faulty selection, after thorough and costly training, the soldier may "break" when he first goes into action. He then, immediately, becomes a permanent and total charge on his government.

In an attempt to forestall such a contingency and to evaluate the examinations given by the Selective Service Boards, a restudy of draftees was recently made by a Board of Psychiatrists. Of those already tentatively accepted, they rejected 29.3 per cent. They estimate that, with proper study, 20 per cent of the draftees may be rejected purely on neuropsychiatric grounds. High as this figure seems, it is far better that the weaklings be weeded out than that the life and usefulness of the soldier be ruined and his country saddled with greater debt.

Many of the physical causes for rejection are remedial, and there is now being made an attempt to salvage some of the rejectees by surgery or otherwise.

The National Research Council is doing a great work in aiding the

Surgeons-General of the Army and Navy Through seven main committees, and their numerous subcommittees, they have been studying various problems for the Army and the Navy

The National Research Council, and the Committee on Medical Preparedness of the American Medical Association, has already accomplished a huge task in classifying every available medical man in the country The old complaint of a round peg in a square hole, so often heard in the last war, should be eliminated almost entirely

Through the many committees of the National Research Council and the National Medical Societies, all the best men in the profession are now acting as most valuable consultants to our military services

It is said, however, that the Surgeon-General does not plan to use consultants in actual combat No individuals stood out more prominently in the Medical Corps of the A E F than those who did so much to enhance the evacuation and surgical care of the "doughboy" No medical officer of the Regular Army but will attest to the valuable services rendered by the consultants in the A E F

The Surgeon-General recognizes that there is no reserve medical personnel in the nation and that none can be developed in a reasonable time The brunt of the burden must be borne by the civil population through a reduction of doctors and nurses These doctors and nurses drawn into the Army must be trained in their extraprofessional responsibilities if they are to discharge their duties to the best interest of the Medical Department

There are actually 11,526 medical officers in Service, ample for the training program, but far short of what will be needed in actual war

Preparations for war are well advanced The training of personnel is well on its way The equipment for modern war is fast coming off the assembly line The production of ambulances, surgical instruments, laboratory equipment, and roentgenologic installations, besides equipment peculiar to Field Service, is proceeding apace

In keeping with the motorization of the Army, the Surgeon-General has developed mobile equipment for surgical hospitals consisting of 14 vehicles, of which seven comprise the operating group

Bus ambulances capable of carrying 12 litter cases, in addition to the more mobile front line ambulances, are being prepared Some of the latter will have light armor protection, carry medical personnel and supplies, and can function as mobile aid stations with facilities to transport casualties

The status of the airplane for rapid evacuation is being studied Army troop transport planes are equipped with devices for securely holding litters, and can be, almost instantly, converted into airplane ambulances But these large planes require landing fields of fair size, so that their effectiveness may be limited The use of the autogyro, that can carry two or three litter cases and needs no landing field, is being investigated

Medical Department personnel, commissioned and enlisted, are being trained for service with parachute troops Their equipment, consisting of litters, splints, dressings, and drugs, have been prepared and packed into

standard containers used by the combat unit for dropping its ammunition, food, *etc*

Hospital trains are being equipped with cars with facilities for rendering medical and surgical care by a completely furnished operating set-up. In addition, each train will have four hospital ward-cars, with beds for 128 patients as well as accommodations for officers and enlisted men.

The program of preparation for National Defense by the Medical Department of the Army is well advanced. The personnel and the equipment have been undergoing severe tests on maneuvers here in the Carolinas.

The experience gained in these maneuvers seems to stress the advantage of younger men in the Army. It is already apparent that many of our own Line officers have passed the age when they are best adapted to the strenuous life of an army campaign. This is undoubtedly true of the Medical Corps as well. Though age, experience and sound judgment will be of great value in the council room, youth must be given the leading rôle in actual combat. In our particular field—surgery—this is of paramount importance. Our young residents, our recent graduates, with adequate postgraduate training, and the junior members of our hospitals and university staffs, will form the surgical teams of this man's Army.

The supply of competent medical officers is now insufficient for our present needs. Many more medical officers will be required. The Surgeon-General has already asked the medical schools to encourage enlistment of their students as members of the Medical Administrative Corps on inactive duty—to be changed over to the Medical Corps proper, when they have graduated and had at least one intern year.

Autocracy is in the saddle again. Again Democracy reels under the all too efficient might of the conqueror. Again we see man's hard-won freedom threatened.

We, in the United States, are guilty of, at least, a share in the failure of the First World War. We must see to it that failure does not occur again.

It was hoped that the Axis Powers could be crushed by the embattled democracies of Europe, with only our material aid. But it is now certain that not only weapons but man power will be needed. Our every effort should be concentrated on seeing that our Army and Navy are well trained and well equipped.

We of the medical profession must see that the armed forces are selected from the cream of our youth.

Again we must see that the fighting man's health is carefully protected.

Again we must see that his medical care is of the best, should he fall ill or should he be wounded.

Every selfish interest in the nation must be subordinated to the great task that lies ahead. Labor must be curbed and forced to assume its true responsibility. Nothing must be allowed to interfere or halt our progress.

The enormous resources of this great nation, her genius for organization and mass production, and last, but far from least, her manhood, can and will win the war.

OXYCEPHALY^{*}

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OXYCEPHALY and its related disorders (acrocephaly, dolichocephaly, scaphocephaly, "tower-skull," Turmschadel, Schadelmissbildung, *etc*) are being considered in this paper. In all of these conditions the sutures may be closed at an early period in life. This leads to malformation of the skull. It may be pointed like a tower, sway-backed, or wedge-shaped. The suture lines close tightly and are obliterated previous to the closure of the anterior fontanelle. This process—*craniostosis*—prevents the proper development of skull and brain. The brain continues to exert marked intracranial pressure in all directions and the skull gives way before the pressure at the point of least resistance, usually most marked in the region of the anterior fontanelle. This fontanelle is the last part of the suture line to close and the bone-margin at this site is the thinnest and least resistant. With the oncoming progressive increase in intracranial pressure, the bony margins are pushed upward, and further ossification takes place about the area of the fontanelle, until, finally, complete ossification occurs. The result is a distorted, misshapen skull, with the most prominent and bulging portion at the site of the fontanelle. Thus, "oxy"—pointed, "cephalus"—head. The head may be elongated and scaphoid with the most prominent protuberance at the same site.

It is not uncommon to see persons with queerly shaped heads who have normal physical and mental capacities, due to arrest of the condition. On the other hand, oxycephalic individuals may never attain adulthood. Why? The simple answer is that premature closure of the suture lines prevents the intracranial space from keeping pace with the actual growth of the brain and its coverings. In other words, the brain outgrows its case and vital functions cease. The brain is not pathologically small, but the intracranial space is. Therefore, the growth and development of the brain is restrained or held back. (Distinction between this condition and that of the microcephalic or mongoloid idiot must be made.)

It is well known that growth of the brain takes place at a rapid rate in the early years. When the brain continues to grow in such cramped quarters, certain symptoms, signs and characteristics make their appearance. (1) Headaches, which may occur at such an early age that they are not recognized, (2) irritability and mental dulness, (3) characteristic convolutional markings and thinning of the skull, with absent or hardly distinguishable suture line sites, (4) thinning of the dura, (5) unusual and abnormal irregularities of the skull involving most frequently and prominently the site of the anterior fontanelle, (6) tremendous increase in intracranial pressure as shown by measurement of the intraventricular pressure and extreme diminution in the

^{*} Read before the Southern Surgical Association, Pinehurst, N C, December 9-11, 1941

size of the ventricles (ventriculograms), (7) bilateral papilledema, followed by atrophy, resulting in failing of vision and blindness, (8) marked bilateral exophthalmos, which may be so extreme and prolonged that loss of the eyes may ensue, and (9) generalized convulsions. If the condition does not become arrested, it progresses gradually, and death ensues.

Although the cranium may be distorted into various forms, some special roentgenologic findings are always present and show great similarity. One of the most distinctive features is the generalized convolutional markings of the bones forming the cranial vault, giving a wavy, billowy appearance like fluffy clouds. This effect is more marked in the lateral view where all bones forming the cranial cavity (with exception of the base) show similar, if not identical, markings. The floors of the middle and posterior fossae are depressed with corresponding depression of the petrous pyramid and ears, and depression, relative lengthening, and narrowing of the sella turcica. The frontal, sphenoid and maxillary sinuses are small. The orbits are blunted and shallow, thus decreasing the orbital capacity. The lower jaw is prognathous and protrudes prominently due to downward displacement of the mandibular fossa.

All of these findings result from the slow, progressive and marked increase of intracranial pressure against slowly retreating, but nonelastic walls of the cranial cavity. In passing, it might be noted that vision fails earlier, and to a greater degree than hearing, because the bony confines of the orbit are more vulnerable than the petrous. In 1936, the author was confronted with this problem. In search of the literature, an operative procedure which would provide adequate relief could *not* be found. In an endeavor to find such a solution, recurring thoughts continually led one back to the basic fact—the intracranial space was too small to allow proper growth and expansion of the brain. The question then arose: How can the cranial cavity be enlarged sufficiently and symmetrically? The problem was solved by the operation which is herewith described. It was conceived and performed first on November 10, 1936, and was described in a preliminary report of the case in November, 1937.

OPERATIVE PROCEDURE

The procedure may be carried out in two stages, as in the first case operated, but the one-stage operation is preferred, provided circumstances permit. With the patient in the prone position, head resting on a proper support, the drapes are sutured to the scalp so as to expose the head from the supra-orbital regions to the external occipital protuberance, and from the concho-temporal sulcus of the one side to that of the other side. A straight, midline incision is made from the hair-line anteriorly backward almost to the external occipital protuberance (Fig 1 A). If deemed necessary, the posterior extremity of the incision can be extended laterally in an oblique direction, forming an inverted Y. The incision extends through all soft parts to the outer table. Bleeding from the scalp is prevented by application of skin clips. The pericranium is readily stripped from the outer table as far as the superior

temporal lines. In this area the pericranium is more adherent, and greater care must be used in freeing it to prevent tearing and fraying of the pericranium, accompanied by bleeding. The entire outer table is thus exposed from supra-orbital regions to the occiput, and from the low temporal region

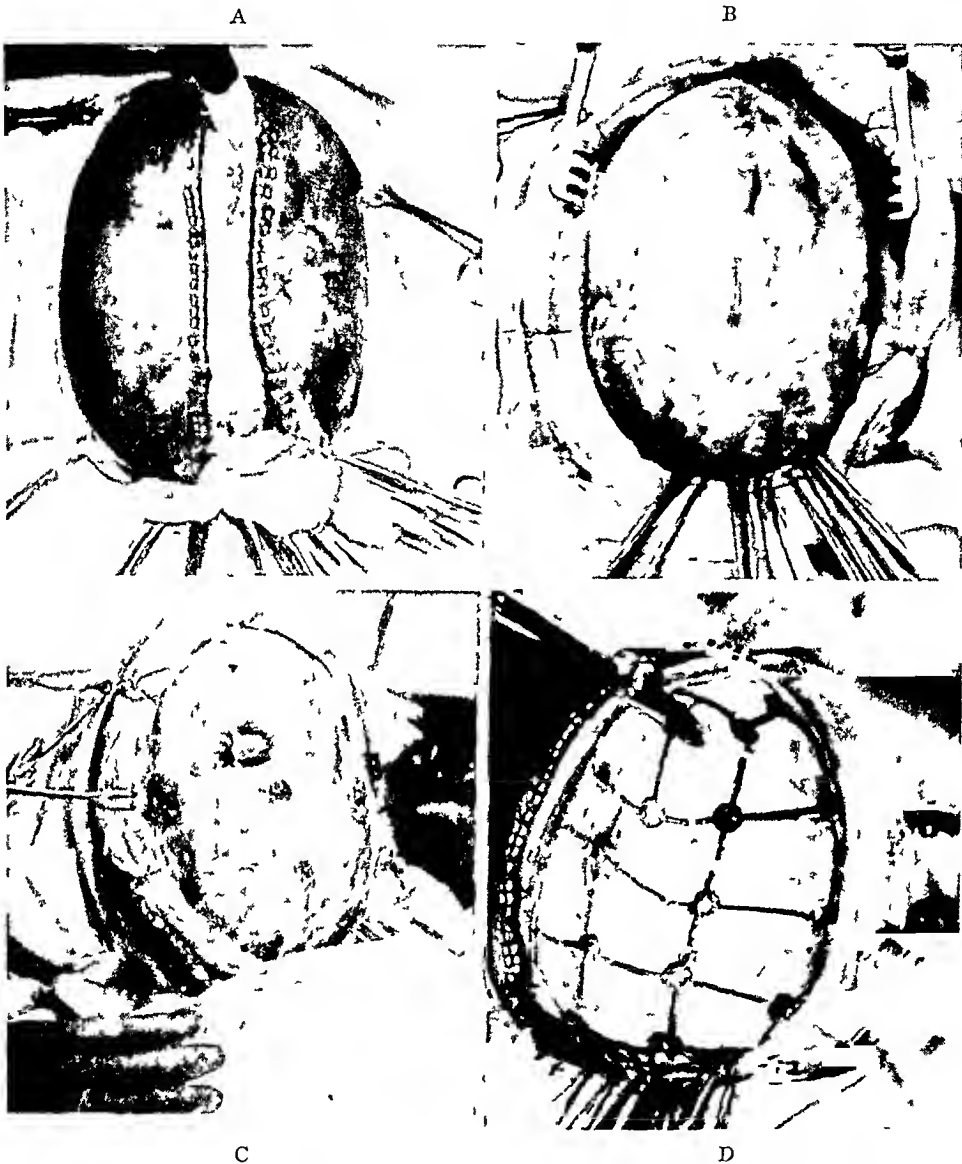


FIG 1—Various stages of the operation (A) Midline straight incision, with inverted Y extension posteriorly. Skin clips used to control bleeding from scalp. (B) Soft parts including pericranium have been reflected exposing outer table of cranium. (C) Circumferential and other bur holes have been made, bleeding from some being controlled by pledgets of cotton. (D) Skull segments cut with deVilliers bone forceps. Segments should be smaller in the area of greatest prominence.

of one side to that of the other (Fig 1 B). The skull may be so thin in areas that it has a bluish-gray tint. Bur-holes are made in a circumferential manner about one and one-half to two inches apart, and similar bur-holes are made throughout the circumscribed area (Fig 1 C). The frontal sinuses offer no problem since they are either absent or quite small. The openings should be placed closer together over and near the most prominent bulging part of

the skull. The bun-holes are then connected with a deVilbiss bone-cutting forceps (Fig. 1 D), or an electrically driven fraise.

When the first groove is cut between two openings, it will be observed that the dura protrudes through the groove similar to the manner in which a towel will "buckle" when two books are placed on it near each other and pushed together. This fact proves redundancy of the dura and sufficiency of the intradural space as compared with the paucity of the intracranial capacity.

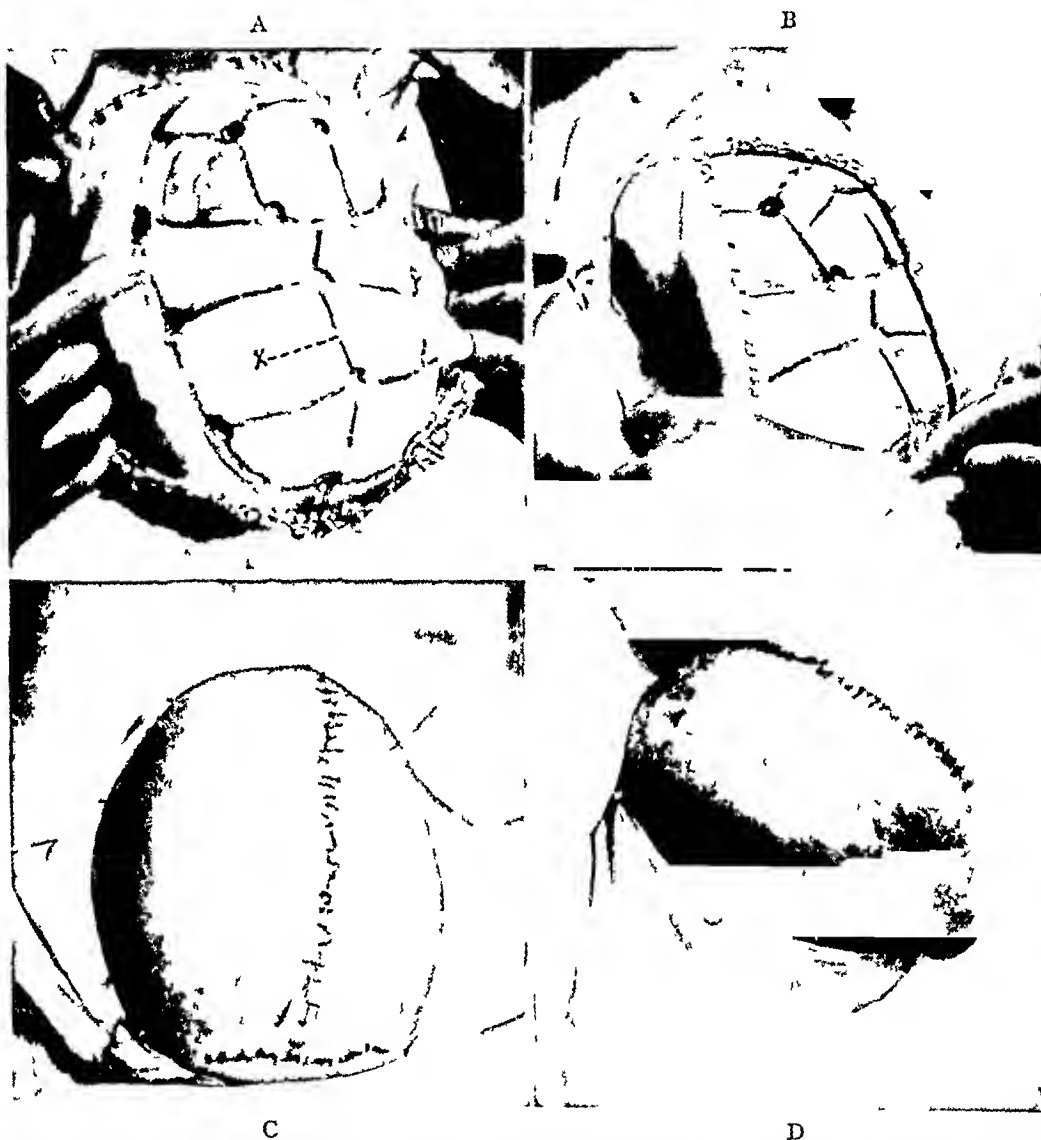


FIG. 2—Concluding steps of the operation. (A) Semilateral view of Figure 1. Small "isthmus" of bone (X) remain while other segments are fashioned and cut through just before closure. (B) Shows separation and elevation of skull segments still attached to the dura. (C and D) Incision closed without drainage.

The dura is quite thin and glistening. When the bone is cut through on three sides leaving the bone flap attached on one side or end, it will be observed that the free end of the bone flap rises and falls like the end of a springboard, with pulsation of the brain. From these two observations it is easy to believe that the brain will expand and reduce the intracranial pressure after all the bun-holes have been connected. This proves to be a fact.

With regard to the shape and size of the skull-segments, it can be said that they should be neither too large nor too small. If they are too large, proper

symmetrical shaping of the skull will not be accomplished, and if they are made too small, too much time will be consumed. Some of the skull-segments will be square, some rectangular, others triangular, trapezoid, *etc*. The skull is thin and cuts readily. In the temporal region the skull may be very thin, like paper, or may even be absent in areas. In the low temporal region it is well to remove the bone entirely with rongeurs, leaving a defect measuring about two inches in the horizontal, and one and one-half inches in the vertical directions, unless the skull is sufficiently large in these areas.

Caution should be employed in two particulars. (1) The dura should *not* be opened, to avoid loss of cerebrospinal fluid. (2) It is well to leave the skull fragments connected by small "isthmus" of bone (the last bite of the deVilbiss forceps) until all of the segments have been fashioned (Fig 2 A). Otherwise, the skull fragments, being insecurely attached to the dura, may slip to the floor and cause embarrassment. The grooves can be cut across the longitudinal sinus with readiness, but, in so doing, "blue" areas, indicating more prominent and embedded portions of the sinus, should be avoided. When all skull segments have been fashioned and cut as desired, the remaining small intervals of bone between adjacent pieces are divided. The intervals, or "grooves," between the various segments increase two or three times in width. The bulging at the site of the anterior fontanelle will disappear completely, provided the skull fragments are sufficiently small over this area. Otherwise the deformity will partially remain.

Bleeding or oozing will be constant from both skull and dura, but the total amount of blood lost is not significant or distressing. The use of bone wax is not advised. It is not necessary, and is a foreign body.

The operation is completed except for closure of the incision (Fig 2 B). This is accomplished by the use of two layers of interrupted silk sutures, one for the pericranium and galea and one for the scalp—without drainage—(Fig 2 C and D). A copious head dressing, including the lower jaw and both ears, is applied without pressure. A light plaster of paris skull cap is placed over the dressing for protection. A small transfusion should be administered.

CASE REPORTS

Cases 1 and 2, operated upon by the author, have been reported, but a résumé of each case will be given, with additional data. Cases 3 and 4 were operated upon by Dr. Barnes Woodhall of Duke University. He has kindly permitted the author to include them in this paper. Although a brief report of these two cases has been made, the completeness of the clinical records justifies a more detailed account.

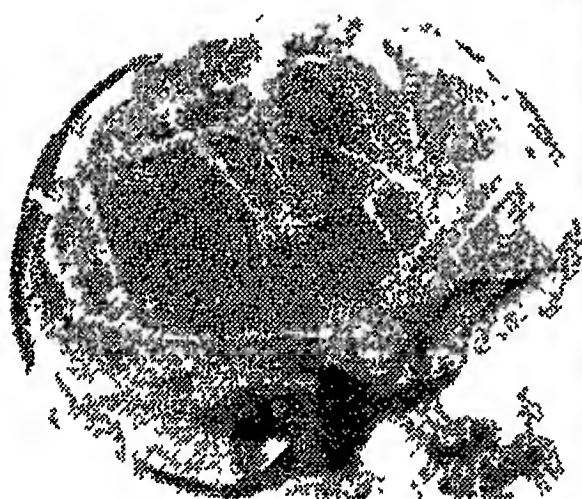
Case 1—E. C., white, male, age 8, was admitted to the Hospital for the Ruptured and Crippled (H23-467), August 10, 1936, for correction of a malunited fracture of right femur. In November, 1935, he had been run over by a truck and sustained a fracture of the right femur. He had been operated upon five times, including plating, without success.

He was fairly well-developed, but rather small for his age. Aside from the deformity of the right femur, the outstanding feature was marked bilateral exophthalmos, with external squint. No ophthalmoplegia (Fig 4 C).

Examination of the right fundus showed marked pallor of the disk. On the left the disk was slightly pink. No papilledema. Pupils reacted to light and accommodation. Mentality fairly good, but he had a somewhat dull, apathetic countenance. General neurologic examination was negative.

A

B



C

D

FIG 3—Case 1—E C (A) Preoperative lateral roentgenogram of skull showing convolutional markings, deep, narrow sella turcica, and other typical findings. (B) Preoperative A.P. view of skull, narrow and pointed above. (C and D) Roentgenograms made February 3, 1937, one week following second stage of the operation. Compare with A and B.

Lumbar puncture showed increased pressure to 400 Mm. of water, reduced to 250 Mm. after removal of 30 cc. of cerebrospinal fluid.

Roentgenograms revealed typical changes in the skull (Fig 3 A and B). Ventriculograms showed small, generally compressed ventricles. Intraventricular pressure was

greatly increased Vision was poor, unable to read, and could barely recognize doctors and nurses standing at the foot of his bed

Upon the request of Dr Philip D Wilson to operate upon the boy, the literature was searched for a method of procedure None seemed to offer much hope for a good result The operation herewith described was conceived and carried out in two stages The first stage was performed November 10, 1936, on the right side Immediately following the first operation there was marked recession of the eyeballs, more on the right side than the left, with improvement in vision Pronounced symmetrical increase in the size of the cranium on the right side was accompanied by widening of the grooves between skull fragments



FIG 4—Case 1—E C (A and B) Roentgenograms made August, 1941, about four and one half years after those shown in Figure 3 C and D, with which compare (C) Photograph of patient before operation (D) Photograph of patient about four years after second stage of operation

Second Stage A similar procedure was carried out on the left side, January 26, 1937, with corresponding increase in size of cranium on that side

Roentgenograms, February 3, 1937 (Fig 3 C and D), showed symmetrical enlargement of the cranium, as desired Softness, or doughiness, of both sides, similar to that of a flaxseed poultice, was present for about two and one-half weeks, followed by slow, gradual stiffening of the cranial vault, until the cranium showed firmness of an ordinary skull (about three months following each stage)

Recovery from both procedures was uneventful Vision improved Successful reduction and correction of malunited fracture of femur was undertaken by Doctor Thompson, December 2, 1936, almost two months following the first stage The patient was discharged, March 17, 1937, and returned to Halifax, Nova Scotia At this time the fundi and vision were practically normal

Letters received from him and his grandmother since his discharge informed us of his return to school and keeping up with his studies He was skating and indulging in activities enjoyed by other boys Roentgenograms of the skull were made from time-to-time Shape and size of skull remained normal No evidence of return of oxycephalic condition

He visited New York in August, 1941 Roentgenograms, made at that time, revealed a normal shaped head on both anteroposterior and lateral views (Fig 4 A and B) The

relative depression of the middle fossa was not so marked. The shape of the sella had completely changed. In the original film, made in 1936, the sella turcica was not only depressed, but was deep and narrow in the anteroposterior direction. In the latest films the sella was normal in contour, being much wider in an anteroposterior direction than in the vertical direction—quite the opposite to the condition seen on the original films. The sphenoid was well developed. New bone had filled the groove lines, also, in both temporal regions from which it had been removed. The upper jaw had developed least of all, and the lower jaw was still prognathous.

Mentally the boy appeared normal. He accompanied the author to a motion picture theater, quickly appreciated all the jokes, and readily perceived the details of the picture without any difficulty at a distance of about 200 feet. He gave all appearances of being a normal individual (Fig 4 D).

Case 2—I. H., Negro, male, age 5, was admitted to Lawrence Hospital (No. 42637), Bronxville, N. Y., October 17, 1940. History of normal birth, 12 children, 7 living. A brother, age 6, showed elongated flattened skull, with prominence in the region of the anterior fontanelle (dolichcephaly), otherwise normal. No other history of malformation of skull in family.

Examination revealed a rather bright, intelligent child for his age. General and neurologic examinations were negative. Lumbar puncture, ventriculograms, encephalograms and electroencephalograms were not considered necessary. There was slight bulging of the eyes, constituting a mild exophthalmos. Intrinsic and extrinsic eye muscles were normal, and eye grounds were normal.

Head was typical "tower-skull," narrow and pointed, more pronounced in the frontoparietal region (site of closed anterior fontanelle). There was apical bulging, elevated about one and one-half inches or more above the surrounding narrow skull (like a haystack) (Fig 5 A and B).

Roentgenograms showed a peculiarly shaped, pointed skull, with convolutional markings and other typical changes (Fig 6 A and B).

In order to prevent mental and visual disturbances which were present in Case 1,



FIG 5—Case 2—I. H. (A and B) Photographs made before operation showing pointed, deformed skull, mild exophthalmos, and protruding lower jaw.

the proposed operation was carried out, October 22, 1940, but in one stage (Figs 1 and 2) During the procedure the same phenomena, *ie*, bulging dura through grooves between skull fragments, pulsation of bone flap, expansion of brain with separation of segments, restoration of contour of skull, etc, were observed When the operation was completed the proper shape of the skull was restored and eyes were less prominent

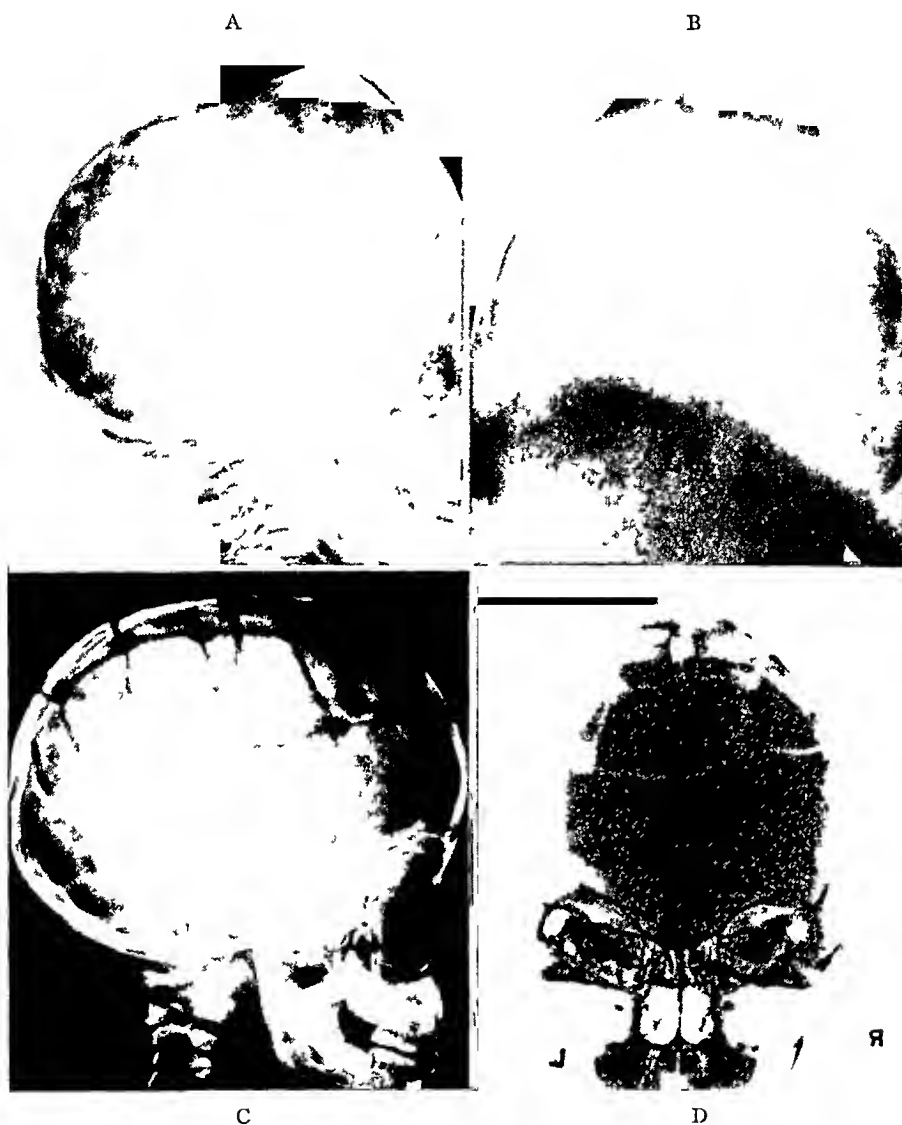


FIG 6—Case 2—I H (A and B) Roentgenograms made before operation Note marked deformity and bulging at site of anterior fontanelle (C and D) Roentgenograms made ten days postoperative showing widening of grooves between skull segments and correction of deformity

Result—The patient had an uneventful recovery Roentgenograms, ten days after operation, showed approximately 17 bur-holes in frontal, parietal and temporal regions, with bone cut between holes, leaving a checker-board appearance in the upper half of the cranial vault The deformity of the upper and anterior portion of the cranial vault, apparent on the original films, had completely disappeared (Fig 6 C and D) There was evidence of solidification of skull as in Case 1 The patient was discharged on the 28th postoperative day, November 19, 1940, and has remained well

More recent films, made in November, 1941, reveal a skull normal in contour, and ossification of the grooves between skull fragments The midline had been crossed at

seven points, and the union of these segments is firm. Convolutional markings in the segments have disappeared, while some evidence of the markings persists in the unsegmented portion of the skull.

Case 3—M. McK. (patient of Dr. Barnes Woodhall), colored, female, age 4, was



FIG 7—Case 3—M. McK. (Operation by Dr. Barnes Woodhall). (A and B) Photographs before operation August 28, 1939, showing marked deformity of head and bilateral exophthalmos. (C) Photographs after second stage of operation. Note almost perfect contour of head and diminution of exophthalmos.



FIG 8—Case 3—M. McK. (A) Preoperative roentgenogram showing characteristic features. (B) Postoperative roentgenogram made following second stage of operation. Note widening of grooves and correction of deformity.

admitted to Duke Hospital, Durham, N. C. (No. A-22502), in August, 1939. Her chief complaints were headaches and eye trouble for two years.

Family history was noncontributory. Past history was negative except for chronic head colds and pneumonia at three years of age.

Present Illness—The mother noted that at birth the patient's head was somewhat distorted. She got along well until two years before admission, when she began to complain of frequent frontal headaches. The child would wake up at night and complain of

severe pain for a few minutes and then fall asleep again. Later she began to complain of headache throughout the day. At the onset of the headaches the mother noticed that the eyes began to protrude, and that they continued to become more prominent until admission. She continued to have severe frontal headache, and, recently, the mother noticed that the child walked with a staggering gait and with a broad base. She did not vomit with the headaches. The mother stated that the child had increasing disturbance of vision.

Physical Examination—Temperature 36.8° F, pulse 92, respirations 20, blood pressure 135/84. The patient was a well-nourished but poorly developed colored female, age 4, who was very cooperative, and did not appear to be acutely ill. The examination was entirely negative except for involvement of the head. Her head was distorted (Fig 7 A and B), approximately normal in diameter in the temporal regions, but over the frontoparietal region the skull came up to a point at the site of the anterior fontanelle and was completely ossified. The anterior and posterior fontanelles were closed. There was marked bilateral exophthalmos. The nose was saddle-shaped, and there was bilateral obstruction to breathing. The hard palate is excessively high, and the lower jaw projects forward considerably.

Neurologic Examination—The patient was mentally clear and very cooperative. All of the cranial nerves were intact. There was some distortion of the optic disks, in that they were oblong in shape. The margins were well outlined. There was no evidence of papilledema. Both disks were slightly pale.

No localized muscular weakness or atrophy was noted. All reflexes were present, equal, and moderately active throughout, except for ankle jerks, which were sluggish. There was no Babinski. No changes were noted to light touch, pain or vibratory sense. Position sense and coordination of movements appeared to be good.

Laboratory Data—Examination of the blood revealed the following: Hemoglobin 73%, RBC 3,340,000, WBC 13,450, Mono 0, LL 5, SL 58%. Urinalysis revealed a slight trace of albumin and an occasional white cell. There were no red cells or casts. Benzidine was negative. Wassermann was negative.

Roentgenograms of skull showed a dolichocephalic skull, with unusual prominence of the frontal bone. There was marked increase of intracranial pressure with typical convolutional markings. All the suture lines were entirely closed (Fig 8 A).

Impression: Cramostenosis. Suggested treatment: Surgical decompression.

On August 29, 1939, a right subtemporal decompression was performed, under bactericidal radiation and avertin-ether anesthesia (Doctor Woodhall). A rather large opening in the skull was made and the dura was opened. Her convalescence from this procedure was quite uneventful, although there was a continual deposition of fluid beneath the subtemporal decompression incision, which had to be aspirated on several occasions.

About this time, the operator became cognizant of the operation for oxycephaly proposed and carried out by the author, and felt that it should be applied in this case. The reason for doing so was the obviously increased intracranial pressure and because of his experience in some ten or 12 previous cases, in which bitemporal decompression had not been particularly effectual in controlling the process. Accordingly, on September 8, 1939, the first stage of the operation proposed by the author was carried out on the right side, the procedure being designated as the "morcellation" operation.

Operation was performed for dolichocephaly (oxycephaly) right side. Dural transplant was performed. Under bactericidal radiation, and avertin-ether anesthesia (by Dr Barnes Woodhall). The effusion under the scalp at the site of the decompression had returned and it was reaspirated at the beginning of the procedure. The entire right half of the scalp was prepared in the usual manner and a sweeping incision made to include the entire right side of the scalp with the mesial border of the incision on the midline. The large flap was turned down without much difficulty, exposing the outer table of the skull on the right side and the site of decompression. The brain was protruding markedly through the subtemporal decompression, and it was quite obvious to the operator that he was correct in assuming that something more had to be undertaken in this particular instance. At this time, a section of the pericranium in the occipital region was dissected

out and sutured in place over the exposed brain in the subtemporal region so that no further effusion of subarachnoid fluid could develop. The entire right side of the skull was then encircled by perforator openings about 4 cm apart, and an inner circle also was made so that the entire right side of the skull could be sectioned in a definite mosaic. The dura was dissected free from the bone, and a mosaic pattern was carried out with the deVilbiss rongeurs. It was not attended with much bleeding. Across the midline, grooves were cut with the deVilbiss forceps in three areas over 3 cm beyond the midline into the left side, where they will be joined within about three months with the mosaic on the left side. The scalp flap was then sutured in place with interrupted fine black silk sutures and the skin was closed with continuous silk. (Before the incision was closed a sketch and natural and color photographs were made.) It was necessary to give the child some glucose and blood during the procedure.

Her convalescence from this operative procedure was quite uneventful, and on September 18—ten days postoperative—a head encasement was applied. She was discharged, September 24, 1939, greatly improved, having no headaches, and having definite recession of the exophthalmos, particularly on the right side.

On October 23, 1939, roentgenograms showed still further separation of the trephine areas, the bone segments in the right parietal region seemingly almost completely separated.

The child was readmitted to Duke Hospital (Hist No 1 C-21946) for the second stage of the operative procedure, at which time she stated that she had continued to be free from headaches and eye disturbances. There was a large, soft bulging of the head in the right temporoparietal region at the site of the original decompression, measuring approximately 12 cm across. On palpation, it was very soft, with no underlying bone palpable except for two small detached fragments anteriorly. In addition to the soft swelling, however, the bony portion of the right side of the skull was definitely fuller, or better filled and rounded out than on the left, where the absence of fullness was quite apparent pathologically. There was only slight, if any, abnormal tension in the bulging area. There was a pronounced exophthalmos on the left and a moderate endophthalmos on the right.

Neurologic examination revealed no papilledema and all cranial nerves were intact. There were no motor or sensory changes and the reflexes were physiologically and bilaterally equal. Head measurements were as follows: Top of ear to top of ear 27 cm; Inion to nasion 35 cm; Greatest circumference of head 51.5 cm.

Exophthalmometer reading with the instrument set at 101: O.D. 23, O.S. 25. Ophthalmoscopic examination through undilated pupils revealed the elliptical disks, which indicate a moderately high degree of astigmatism. Retinal vessels were normal. There was no congestion of retinal veins. The peripheral fundi were normal. The maculae stood out rather distinctly. Vision with the illiterate chart was approximately 20/40 in each eye.

Because of an acute rhinopharyngitis the second stage of the operation was delayed until January 19, 1940, when all symptoms had disappeared.

The second stage of the operation was undertaken January 19, 1940. It was carried out in a similar manner to that of the right, except for the fact that there was no decompression site to be dealt with, also, the grooves could not be carried across the midline with the de Vilbiss forceps because of marked venous bleeding which developed in this region and for fear of damage to the longitudinal sinus. Nevertheless, there was noticeable separation of the bony incisions and actual distention of the hemisphere on the left side. The incision was closed as at the first stage.

Postoperative course was uneventful. On January 30, 11 days postoperative, a head encasement was applied, and the patient was discharged (Fig 7 C). On April 10, 1940, she returned for observation. The mother stated that the child had become really a new child, had no headache, and appeared to have no visual disturbance. The head measurements showed the greatest circumference 53 cm, top of ear to top of ear 28 cm, and inion to nasion 37 cm. Exophthalmometer readings were 28 bilaterally, set at 113.

The patient returned on May 27, 1941. She had had an uneventful course since the last operation. She had no headaches, no convulsions, normal vision, normal speech, and normal mentality. The mother stated that the child had acted very much like a normal child should. Her head measurements showed the greatest circumference of 55.5 cm as compared with the preoperative measurement of 51.5 cm.

Examination of roentgenographic films of the skull in comparison with those of October 23, 1939 (Fig 8 A and B) showed practically complete union of the bone fragments except in the frontoparietal regions and the occipital region, and in these regions some bony union appeared to be taking place. There was also some disappearance of the convolutional atrophy previously noted. Some general filling-out of the cranial vault had taken place, and it was more normal in contour than on previous films. It was noted that the present appearance, all-in-all, was a decided improvement over that of 1939. This opinion was substantiated by the operator's observations and the observations of the nurses on the pediatric ward, who had followed the child for two years. Peripheral visual fields, taken at the time, showed normal findings.

On account of living near the hospital she was to be followed during later years.

Case 4—T. C. (patient of Dr. Barnes Woodhall), white, female, age 14, was admitted to Duke Hospital, Durham, N. C. (Hist. No. A-41861), June 5, 1940. Chief complaint: Convulsions, ten months' duration.

Family and past history were noncontributory. **Present Illness.** The patient was born with a peculiarly shaped head and protruding eyes. She had always been nearsighted, and was somewhat small for her age. Other than this the child behaved well until ten months prior to admission when she began to have convulsions characterized by cyanosis, unconsciousness, urinary incontinence and drawing of hands and legs. These attacks occurred five or six times a night.

Physical examination was negative except for head. There was a marked bilateral exophthalmos. The upper lip was somewhat undershot and the nose had a definite hook to it. All the features were characteristic of oxycephaly. The head itself was small in all diameters, somewhat flattened posteriorly, and of striking interest was the presence of a smooth bulge in the region of the anterior fontanelle. This bulge measured about 4 or 5 cm in diameter. The optic disks were hazy and were interpreted as being indicative of mild increase of intracranial pressure. Vision was 20/200 in the right eye and 20/400 in the left eye. There was mild generalized constriction of both visual fields.

Stereoscopic roentgenograms of the skull showed oxycephaly with marked increase in intracranial pressure, as evidenced by the convolutional markings with none of the suture lines being present (Fig 10 A). The sella was not enlarged but was unusually deep. (This corresponds with the findings in other cases of oxycephaly.) The narrowing and deepening of the sella were interpreted as also being due to pressure.

A lumbar puncture was performed and encephalograms made. The initial manometric reading was 220 mm of water. The encephalograms showed typical findings, i. e., marked diminution in the size of the ventricular system, without loss of ventricular symmetry. Spinal fluid showed total proteins of 18 mg. % Blood Wassermann and Kahn reactions negative, as was the spinal fluid Wassermann. An electroencephalogram showed the presence of *delta* waves over the entire cortex, indicating diffusely increased intracranial pressure. The patient was discharged and preparations were made for operation.

She was readmitted to Duke Hospital, November 4, 1940. Endocrine examination showed oxycephaly, marked bilateral exophthalmos (Fig 9 A), retarded statural growth, partially retarded sexual maturation, headaches and convulsions. The conclusion was secondary hypopituitarism due to increased intracranial pressure incident to oxycephaly. Intelligence tests revealed the patient to be a low-grade moron. Prognosis for future development was not good.

Head measurements showed the circumference 49.5 cm, diameter frominion to glabella 15 cm, lateral diameter from one superior conchotemporal fold to the other

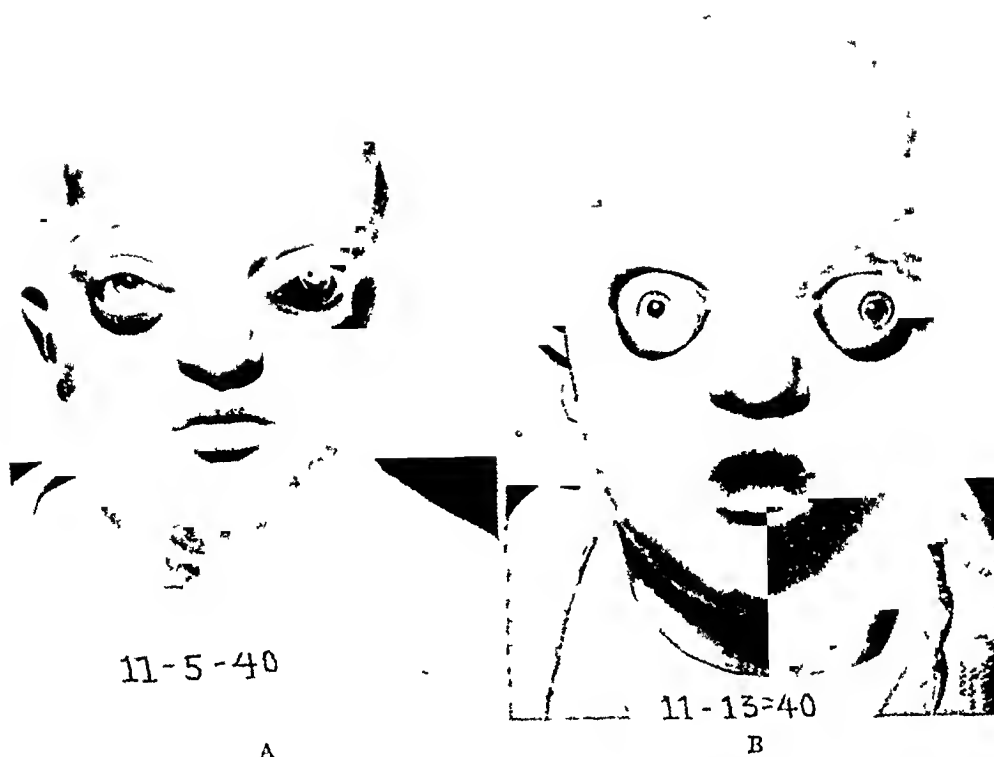


FIG 9—Case 4—T C (Operation by Dr Barnes Woodhall) (A and B) Pre operative photographs showing extreme exophthalmos and dull countenance



FIG 10—Case 4—T C (A) Preoperative roentgenogram after air injection. Note very small compressed ventricular system. (B) Roentgenogram made about 11 days after the second stage of the operation. Note separation of skull fragments, the new growth of bone in the skull defect in the right subtemporal region, and correction of deformity

12.5 cm. Exophthalmometer readings, with the instrument set at 112, were 26 Mm in both eyes, visual fields considerably constricted. Visual studies showed 20/400 in the right eye and 10/400 in the left eye. Both fields were considerably more constricted than at the time of the last admission, almost down to the point of macula vision in the left eye. Audiograms disclosed normal hearing in both ears. An electroencephalogram showed slow enlarged and misformed waves abundant over all regions during the resting state, being most marked over the right occipital region.

On November 13, a photograph was made showing extreme exophthalmos with protrusion of both eyeballs beyond both lids, in fact, the under surface of each eyeball was in contact with the skin overlying the lower rim of the orbit (Fig 9 B).

On this date operation was carried out on the right side by Doctor Woodhall, in the usual manner. Bone was removed from the right subtemporal region, but the dura was not opened. The dura expanded markedly through the bony defect. Morcellation was carried out. The resulting expansion was more marked than observed in Case 3. Immediately following completion of the dressing and application of the bandage, it was quite remarkable to see the diminution of the exophthalmos involving the right eye, whereas the left eye remained protuberant.

An electro-encephalogram made December 13, one month postoperative, showed the amplitude of the waves within normal limits throughout the entire record, a marked improvement—normalization—of the electroactivity compared with the record of November 5.

At discharge, December 14, direct vision was 20/200 in the right eye and 20/400 in the left. Circumference of head in horizontal plane was 49.5 cm preoperative, and 50.5 cm postoperative, in the sagittal plane 28 cm preoperative, and 28 cm postoperative, in the coronal plane 27 cm preoperative, and 28 cm postoperative. With the ophthalmometer set at 112, preoperatively, both eyes show 26 Mm. Postoperatively, the ophthalmometer set at 108 showed 24 Mm both eyes. The patient was to return at three-month intervals for observation.

Patient was readmitted to Duke Hospital, August 24, 1941, for the second stage of the operation. It was noted that the patient had not had any convulsions since the first operation, and headaches have been very mild.

Plain roentgenograms of the skull showed definite evidence of healing, particularly over the transverse resection areas and in the subtemporal area. Where the bone had been completely removed, almost one-third was covered by new bone. This was perfectly obvious upon palpation of the defect.

The second stage of the operation was carried out on the left side, by Doctor Woodhall, under bactericidal radiation. Avertin-ether anesthesia was used. The bone was completely removed in the low temporal squama as was done on the right side. Marked increased intracranial pressure was evident with elevation and separation of the individual skull segments. The scalp incision was closed. The patient's condition was excellent throughout the operation, followed by uneventful healing of the wound (Fig 11 A and B).

Postoperative electro-encephalography showed irregular waves of not enlarged amplitude and of continuously changing frequency over all regions. Pathologic forms absent. No *alpha* rhythm was present. Overventilation, in contrast to the former examination, has no influence upon the pattern. No special irregularities in the right parieto-occipital region were evident. The record was regarded as within the range of normal.

Head measurements following operation. Circumference 53 cm, nasion toinion 33 cm. Postoperative roentgenograms were made (Fig 10 B).

Psychometric examination was carried out at this time, and indicated an improvement in the patient's mental condition and behavior. She showed more confidence in herself and the tempo did not appear so retarded.

Doctor Woodhall's final statement about this patient follows: "To this date, it is my impression that the child has been definitely improved by the two-stage operation upon the skull. A glance at her photographs on November 5, 1940, as compared with Sep-

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tember 1 1941 shows I believe a definite change in the child's appearance and certainly in the amount of exophthalmos. The child can no longer protrude the eyeballs in her gruesome manner. Electro-encephalograms show very definite release of pressure and we have been very pleased with the cessation of her convulsions without any type of anticonvulsant therapy. Finally although the psychometric test is somewhat discouraging at least she has progressed with her age-group although she is starting at a low level. The social service workers in Greensboro are planning to place her in school for the first time in her life and the child herself is very eager to start her learning. The author believes that this patient's mentality might not have been so impaired had it been possible for this operation for oxycephaly to have been performed when she was three or four years of age.



FIG 11—Case 4—T C (A and B) Photographs made several days after the completion of the second stage of the operation. Exophthalmos considerably lessened.

Doctor Woodhall has completed a third case, and has performed the first stage upon two other cases, but he did not consider that these cases were ready for presenting at this time. Dr R. F. Slaughter, of Augusta, Ga., performed this operation in three cases and stated that improvement followed operation in each case.

In addition to the characteristic changes associated with oxycephaly, all cases showed some degree of hypopituitarism, more marked in the older children. It is suggested that this condition is due to the constant and prolonged increase of intracranial pressure exerted on the pituitary body and the sella turcica. In all cases before operation, roentgenograms showed deep, narrow sellae. In Case 1, observed for a period of five years since the operation, the present roentgenograms reveal a sella normal in appearance, much wider in the transverse than in the vertical diameter, in contrast to the reverse measurements in the preoperative films. In a discussion, it has also been suggested that the healing of the malunited fracture (pseudo-arthritis) subsequent to the open reduction performed after the first stage of the operation for oxycephaly in Case 1, after failing to occur preoperatively following performance of five operations for the same condition in the femur, was connected in some way with a changed condition in the pituitary body. It was considered that this change in the function of the pituitary body might have

resulted from the relief of the compression of the pituitary body by the wide decompressive effect afforded by the operation. This suggestion is made as a possibility, and not as a firm belief.

Sufficient evidence is presented to warrant the use of this operation in cases of true oxycephaly. It is advised that the operation be done before failure of vision and marked changes in mentality occur. This procedure may be of value in microcephaly. It might also be of value in the treatment of children with partial obstruction of the aqueduct accompanied by a mild degree of internal hydrocephalus, as suggested by the marked increase in the size of the skull in arrested cases which reach adulthood.

SUMMARY AND CONCLUSIONS

(1) Oxycephaly and allied conditions of the skull due to premature closure of the suture lines, without operation, terminate in blindness, dulled mentality and death, unless spontaneous arrest of the condition intervenes.

(2) An operation was proposed by the author, and performed for the first time in 1936. This operation may be undertaken in two stages, or in one stage, if circumstances permit.

(3) A description of the operation is given.

(4) A report of four cases is made. Case 1 was operated upon five years ago. A brief follow-up report of this case is made, substantiating beliefs stated in the preliminary report published in 1938. Immediate improvement has followed in all cases operated upon.

(5) Reference is made to other cases improved by operation, but not reported in this paper.

(6) Hypopituitarism associated with these conditions may be affected by the diminution of the increased intracranial pressure afforded by the operation.

(7) The procedure is *not* advocated in cases of microcephaly, or idiocy.

(8) Good results should follow performance of this operation in cases of *true* oxycephaly.

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DISCUSSION—DR BARNES WOODHALL (Durham, N C) We have had the opportunity of operating upon three children with oxycephaly, using the procedure described by Doctor King We have been pleased with our results as compared with those obtained previously with the use of subtemporal decompression In all cases, the vertex deformity so characteristic of oxycephaly has been obliterated and a normal contour of the skull has been re-established In each instance the circumference of the skull has increased, the increase following operation in one case measuring some 4.5 cm The most striking evidence of the relief of increased intracranial pressure by morcellation of the skull is found in a comparative study of electro-encephalograms taken before and after operation Before operation, studies of cortical activity show distorted forms with unstable frequencies, with large three-per-second waves in all leads Following operation the records have returned to normal In each case, the diminution in visual acuity, which may be so profound in oxycephaly, has been checked over a postoperative period of observation of some two and one-half years, and in one instance vision has improved In one case, convulsions which had been present for a period of some ten months prior to operation ceased following operation and have remained absent for a period of 11 months without any other type of anticonvulsant therapy Finally, the parents of these children affirm that they have ceased to complain of headache and visual loss and they are much more normal in every respect

In our observation of some five cases recently, we have recognized two distinct forms The first is that of true oxycephaly, with the characteristic deformity associated with a beak-like nose, hypoplasia of the maxilla, prognathism and occasionally with deformities elsewhere in the body The second type is the so-called delayed oxycephaly, with the characteristic deformity and skull changes without the other features of true oxycephaly

In our colored slides I have endeavored to illustrate this second type of oxycephaly The first stage morcellation of the skull as carried out by us is also illustrated We have not seen fit to undertake the procedure in one stage in these older children but, undoubtedly, as Doctor King has pointed out, a one-stage procedure could be advantageously and safely carried out in an earlier and younger case In our experience, morcellation of the skull appears to be an ideal procedure for the relief of oxycephaly

TREATMENT OF COMPOUND FRACTURES OF THE SKULL *

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THE PURPOSE of this paper is to emphasize the importance of early operation in the prevention of infection and to discuss certain technical procedures which, from personal experience, have been found most effective in the treatment of compound fractures of the vault of the skull

The discussion does not include fracture of the base of the skull which is usually compound through the cranial sinuses, nor penetrating wounds produced by gunshot or other agents. The situation created by compound fractures of the base of the skull, because of their usual inaccessibility, is often a most complex one, totally unfavorable to effective surgery

The frequency of open wounds of the head and the benefits of surgery in the prevention of infection give to these wounds an importance far exceeding that of any other surgical lesion produced by head trauma. Open fractures of the vault of the skull should present few problems of management to those familiar with such injuries but unfortunately they are often inadequately treated

The prevention of infection is dependent on removal of contamination by early operation, and we believe there should be no delay in disinfecting these wounds beyond that necessitated by the patient's general condition. A delay of more than eight hours is rarely required. If infection is prevented the mortality is low, cerebral scarring is minimized, and epilepsy as a late result is much less likely to develop

The principle of early, thorough operation within the first few hours after injury has been widely accepted as fundamental in the management of these cases, but there is not complete agreement. Review of recent literature discloses that a delay of 24 to 48 hours between the injury and operation is recommended by Munro,¹ in all cases of compound fracture of the skull. If operation is not undertaken within 48 hours, he advocates a further delay of from three to six months. It seems difficult to justify a delay of at least 24 hours in all cases when surely infection will develop in many of these contaminated wounds and may lead to fatal intracranial complications. We can see little reason for operation upon those who survive three to six months unless perhaps as a belated effort to prevent or control epilepsy or to eradicate osteomyelitis. Certainly, it would seem that the opportunity for rendering the greatest service to the patient may be lost by delay. It being impossible to predict the hour when infection will begin in a contaminated wound, the only safe course in such an uncertain situation is to remove those factors which lead to infection as soon as the patient's condition permits. It is true that chemotherapy may retard the onset of infection but the sulfonamide agents

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should be considered merely a supplement to, and in no sense a substitute for, early, adequate surgical treatment

It should not be assumed that patients with compound fracture of the skull are necessarily in a state of shock. Many of them with crushing fractures of the vault and extrusion of pulped brain tissue through the scalp laceration are conscious, alert, and in good general condition on admission to the hospital. Shock may be present from loss of blood or severe associated injuries but an analysis of a large series of consecutive head injury cases in my clinic has shown that the incidence of shock, as determined by clinical observations and blood pressure readings, was less than 10 per cent of the total number admitted to the hospital. When the injury is confined to the head shock is even more unusual. A high percentage of compound fractures, therefore, may be safely operated upon within the first eight hours, and our records show no instance of shock developing from early operation for compound fracture of the skull. We do not fix an arbitrary time limit for operation in cases when delay is unavoidable from shock due to associated injuries or late admission of the patient to the hospital. These cases must be individualized and some of them, if given early chemotherapy, may be successfully operated upon for the prevention of infection at a much later period than was formerly thought possible. Success of delayed operation in some of these cases, when such delay is absolutely necessary, in no way invalidates the arguments for early operative treatment in patients whose general condition is good and, in our experience, the large majority fall in this class.

When shock is present the treatment obviously should be directed to this condition and except for the arrest of external hemorrhage by simple means, no local surgical treatment of the head wound is permissible. The hair should be clipped about the laceration, sulfanilamide powder freely dusted in the wound and a sterile bandage applied. Transfusion may be necessary. It is of the greatest importance that shock is not increased either by ill advised surgery of the head wound or the injudicious management of associated injuries. Manipulation of fractured long bones, unnecessary handling of the patient or roentgenologic examination should be postponed until the patient has recovered from shock.

Operation for compound fracture of the skull will vary from disinfection, debridement and suture of the scalp laceration overlying a compound linear fracture, to a very extensive procedure in severe cases with brain laceration from indriven fragments of bone, requiring thorough debridement of scalp, bone, dura, and brain. However, the underlying principles of treatment are the same in all open wounds of the head.

Thorough disinfection and debridement of scalp lacerations are most important features of the operative technic of compound fractures. Some years ago we substituted irrigation with normal saline or Ringer's solution for chemicals in the disinfection of simple scalp lacerations. The effectiveness of mechanical removal of contamination by large quantities of nonirritating solution was amply demonstrated by Cushing² in the treatment of penetrating brain wounds.

during the First World War. His results had much to do with the adoption of similar methods for disinfection of the associated scalp and bone injury.

Roentgenologic examination, which is a routine preliminary to operation, may show marked depression of the bone fragments. Extruded brain tissue is often seen matting the hair about the scalp wound. Patients with a crushing fracture in the frontal region and severe damage to the brain from indriven fragments of bone are frequently conscious on admission. The state of consciousness in these cases may be contrasted with that in more common types of injury in which the patients receive a heavy blow on the head which may or may not produce a linear fracture but does cause immediate and more or less prolonged unconsciousness. The explanation of retention of consciousness in cases of depressed fracture may well lie in the fact that the giving way of bone in the depressed fractures acts as a shock absorber to the impact and restricts the effects of the concussion force to the region of the injury.

Local anesthesia should be used whenever this is practicable, and we do not hesitate to give morphine to quiet a restless patient at the time of operation if the examination does not indicate increased intracranial pressure. Intracranial pressure is often spontaneously relieved in cases with lacerated dura by the extrusion of blood clot and pulpified brain tissue. Iodine and alcohol may be applied around but not used in the wound. Novocain solution, 1 per cent, with three drops of adrenalin to the ounce of solution, is then injected in the scalp around the wound. The scalp laceration should be freely irrigated with Ringer's or saline solution and the laceration débrided back from its edge for at least one-eighth inch. After this is done the wound is again irrigated. The fracture should be carefully inspected and if it does not appear to be contaminated and is not depressed, no treatment of the fracture line is indicated. In some cases there may be obvious contamination of the fracture line with foreign matter such as hair and grit caught between the bone fragments. When such is the case it is necessary to excise the contaminated fracture line with a narrow rongeur to permit complete disinfection of the wound. The suture of a disinfected scalp laceration, usually considered a minor procedure, has been called by Colonel Cairns, of the British Army "the most important cranial operation of war." After complete disinfection and débridement the scalp laceration is sutured in all cases in two layers with interrupted fine silk sutures. The whole treatment of compound linear fractures in the large majority of cases consists merely of adequate disinfection, débridement and suture of the overlying scalp laceration.

It may be necessary to enlarge the scalp wound after it has been disinfected and débrided in order to give better access to the fracture. When the fracture is exposed the depressed fragments often may be removed with little difficulty but in some cases the fragments are locked and require a bur-opening adjacent to one of the fracture lines and the rongeur away of a small area of bone to free the impacted fragments.

Usually there is very little hemorrhage in removing the bone fragments but when the fracture overlies a large venous sinus one must proceed cau-

tiously and be prepared to deal with formidable hemorrhage should one of the venous sinuses be punctured by a spicule of bone. The application of muscle grafts is the most effective way to control hemorrhage from one of these sinuses but much blood loss may result before the bleeding is stopped. In one such recent case the patient was practically exsanguinated on admission and died from hemorrhage from the sinus before the laceration of the sinus could be exposed.

If the exposed dura shows no laceration, one should attempt to determine whether there is underlying hemorrhage caused by the fracture. A bluish discoloration of the dura indicates there is subdural bleeding and if operation is undertaken early after injury it may be safe to open the dura and remove the clot and macerated brain tissue by irrigation and suction. However, if there is doubt as to the completeness of disinfection of the wound, the dura should not be opened unless demanded by evidence of considerable subdural bleeding which would necessitate the removal of accumulated blood and control of subdural hemorrhage.

There is no general agreement regarding replacement of bone fragments in compound fractures of the skull. In some cases we have replaced the fragments on the dura with firm healing in a few weeks. The chances for healing of the replaced fragments without infection are perhaps increased with chemotherapy but if one is not reasonably sure that they are free of contamination, or if the operation has been delayed beyond 12 hours, it would seem best to discard the fragments. As a rule, it is inadvisable to replace the fragments when there has been laceration of the dura with severe injury to the brain.

When the dura is lacerated and there is localized injury to the brain, the macerated brain tissue, blood clot and other loose debris may be removed by irrigation and the suction force of a bulb syringe, but this can be done more effectively with the suction apparatus. With about eight to ten pounds of suction pressure, all lacerated tissue and blood clot can be removed down to the healthy brain tissue. This may be done under direct inspection even though the brain wound reaches a considerable depth. In some cases, penetration by spicules of bone causes a subcortical hemorrhage, which leaves a cavity of moderate size in the brain after the clot has been removed. With a lighted spatula the brain wound may be inspected in all of its recesses for the removal of debris and exposure of bleeding vessels. Hemorrhage is controlled by coagulating the vessels with the electrosurgical unit after drawing them into a glass suction tip. This is a most satisfactory method of dealing with hemorrhage in the depths of a brain laceration. After the brain wound is thoroughly cleansed by irrigation and suction, and all bleeding arrested, it is filled with Ringer's solution. We make a practice of closing the dura in all cases. It may be necessary to use a small graft of pericranium, galea or temporal fascia or even fascia lata to secure tight closure. Repeated irrigations are required throughout the operative procedure for compound fractures of the skull.

Crushing fractures of the skull in the frontal region frequently involve one

or both frontal sinuses and the fracture line may radiate along the base through the ethmoid and sphenoid sinuses. Fracture through the frontal sinus is of no especial significance in the production of early infection unless the adjacent dura is lacerated. Should the sinus later become infected, the patient would be exposed to the same intracranial complications as may follow sinus infection from any cause. In many cases of compound vault fractures there is marked comminution of the wall of the frontal sinus with extensive laceration of the dura adjacent to the sinus and under the frontal lobe, from fractures radiating backward through the ethmoid. The procedure we have followed in such cases is, first to disinfect thoroughly the scalp laceration and brain wound, then repair the dura securely. After tight closure of the dura, using a graft if necessary, the detached bone of the sinus wall and the mucous membrane should be completely removed. The sinus is then packed with iodoform gauze. No drainage material is inserted into the dura in the treatment of any type of compound fracture, and, in our opinion, it should be avoided, especially when the fractures involve the frontal sinus.

There appears to be no uniform practice with respect to intradural drainage in severe fractures of the vault involving the frontal sinus. Cone³ recommends intradural drainage with the drain emerging in the lower anterior temporal region. Munro⁴ inserts a conical wire mesh drain through the dural laceration into the defect made by "cortical excision." We have acted on the belief that cases involving the frontal sinus and requiring operation on the sinus are especially unfavorable for any drainage material which passes into the dura. Assuming that the brain wound has been thoroughly disinfected, it appears to the writer that the most important step in the technic of operation in these cases is the secure closure of the dura without drainage. In all cases in which the dura has been opened, we start sulfamidamide promptly but we have not used it locally within the dura in any type of intracranial operation.

In compound fracture of the vault with radiation of the fracture lines through the frontal and ethmoid sinuses, a cerebrospinal fluid leak may persist from faulty repair of accessible dural lacerations and also in cases in which the tear of the dura is inaccessible. The sole surgical indication in fractures of the base of the skull is to close a cerebrospinal fluid leak. These injuries are not considered in this paper but it may be mentioned that we use chemotherapy promptly in all cases with leaking cerebrospinal fluid from any cause. Chemotherapy will very likely obviate, to a great extent, the necessity of operation in cerebrospinal rhinorrhea from basal fractures.

The same nursing care is required for patients after operation for compound fracture as for any other type of severe head trauma. In cases with pulmonary complications it may be necessary to keep the patient in a lateral prone position with the foot of the bed elevated for a considerable part of the time to relieve obstruction of the air passages by bronchial secretions. Infection should be prevented in practically every case of compound fracture of the

skull, and the results of operation for compound depressed fracture with laceration of the dura and extravasation of brain tissue are surprisingly good.

In a series of more than 2,000 consecutive head injuries admitted to the hospitals of the Medical College of Virginia from 1935 to 1940, inclusive, there were 224 compound fractures of the skull, with a gross mortality rate of 16.5 per cent. Of this number, operation upon the skull for depressed fracture or contaminated linear fracture was necessary in 105 cases, with an operative mortality of 11.4 per cent. Of the entire group of 224 fracture cases there were 40 with severe associated injuries not including those of the facial bones. As was to be expected, the highest mortality was found in this latter group.

A cranial defect of considerable size may result from the operative treatment of compound depressed fractures. For many years we have repaired cranial defects for deformity in the frontal region, and because of the patient's fear of injury to the unprotected area, or when certain subjective symptoms are present which might be attributed to fluctuation of the brain mass from sudden change of position.

After a rather extensive and disappointing experience with the use of thin bone grafts from the outer table of the skull, we have used thick, perforated celluloid plates with excellent results as a substitute for autogenous grafts.⁷ Celluloid plates may be molded to the contour of the skull by boiling the plates between the curved surfaces of two bowls. We have seen only one infection from celluloid plate in a large series of cases and this infection resulted from its application over a defect which involved the frontal sinus. A cranial defect should not be repaired until several months after the wound has completely healed. Intracranial pressure and retained foreign bodies are well known contraindications to cranioplasty. Vitalium⁶ and other foreign materials have been used for cranioplasty but they appear to possess no advantage over celluloid.⁴

Cranioplasty with autogenous grafts from the outer table of the skull was described by the writer⁵ in 1919. This report was based on a large series of cases operated on in the Cape May Hospital (U.S.A. Hosp. No. 11). The end-results of only a small number of these patients are known but it was clearly evident from those examined after their discharge from the army that this type of cranioplasty was unsatisfactory or a complete failure in many cases. Many autogenous grafts fail to survive and of those that do, there is usually sagging in large defects of the vertex. A very serious objection to autogenous grafts from the outer table of the skull is that it requires a tedious and difficult operation to procure the graft. I know of no operation which has less precision or may be more annoying than an attempt to remove the outer table of the skull to repair a large defect. In addition to the difficulties

* The use of celluloid plate for the repair of cranial defects was described by Dr William Perrin Nicolson at a meeting of this Association in 1904. At another meeting, 20 years ago in this hotel, Doctor Nicolson made further reference to the advantages of celluloid plate in the repair of cranial defects, stating it had been used by him constantly since his first report. In a rather humorous way, Doctor Nicolson stated, "The only surgical objection I know to its employment is the fact that it is too easy and simple to do."

of the procedure, one must seriously question the propriety of a prolonged session on the skull of a live human being with a hammer and chisel

Sections of ribs have been used to repair cranial defects. When the defect is in the frontal region, repair with rib or rib cartilage is unsatisfactory from a cosmetic standpoint and cranioplasty by this method is also a troublesome procedure. Among the autogenous grafts, perhaps those from the ilium are the most satisfactory.

Except for its cosmetic effect, the relief of certain subjective symptoms and the sense of protection it gives the patient, there is no other indication for the repair of cranial defects. We believe that all of these indications for cranioplasty can be met by the use of celluloid plate and there seems little justification for doing a long, tedious procedure when a more simple one will suffice.

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DISCUSSION—DR CHALMERS H. MOORE (Birmingham, Ala.) Doctor Coleman's discussion of compound skull fracture was of especial interest to me for two reasons. First, our methods have been diametrically opposite, and second, because our results very nearly parallel each other. We have preferred to consider that the great majority of these cases are either in shock at the time of admission, or in potential shock. If operation is undertaken too early, one never knows to what depths he may have to go, and a potentially shocked patient may well be carried into profound shock. To be sure, there is local infection present at the time of injury, but the bacteria do not spread through the tissues in 24 hours. The results following delayed operation, considering sepsis as the primary problem, have shown a greatly reduced mortality rate, the incidence of infection is not more than 3 per cent, and that has been reduced by the use of sulfanilamide. We do not hesitate to fill the wound with powder.

The lacerated scalp wound is inspected, and the sterile finger used to determine the presence of an underlying fracture. This is more definite than the roentgenogram. If the skull is fractured, nothing more is then done except to fill the wound with sulfanilamide, apply a dry dressing, and institute treatment for shock if necessary. Twenty-four hours following injury is the optimum time to operate, there is no need to wait past that time unless of course some contraindication exists, such as severe associated injury. This is often the case. If necessary to postpone operation beyond 48 hours we, with Munro, have reached the conclusion that it is better to let the wound heal by granulation and carry out any necessary operative procedures several months later.

We feel very strongly that many instances of potential shock will be prevented from going into profound shock by waiting 24 hours.

RECENT ADVANCES IN THE DIAGNOSIS AND TREATMENT OF RUPTURED INTERVERTEBRAL DISKS *

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THERE can be few more remarkable examples of the excellent results that accrue from intelligent intensive cultivation of a surgical field than that of ruptured intervertebral disks. Twelve years ago a ruptured intervertebral disk was unknown¹. Now it is a clinical entity, with precise definition, surprisingly common, and curable by operative means, without risk or loss of bony structure. Neurosurgeons now see more ruptured intervertebral disks than any other lesion.

This entity accounts for an overwhelming percentage of the hitherto incurable and untreatable low back pains and sciaticas, and mis-called sacro-iliac strains, arthritis of the spine, *etc*—all of which must have been anathema to orthopedists. To have reached the present stage in diagnosis, it is to be expected that many diagnostic tests should have been introduced and subsequently become unnecessary. And it is equally obvious that the operative treatment should have become greatly simplified.

At first, this lesion was localized by injecting small amounts of lipiodol into the spinal canal. For the detection of the smaller protruding disks by filling defects, large amounts (5 cc) of this substance were introduced by Mixter and Barr² (1934). Unless subsequently removed, lipiodol is a permanent deposit in the subarachnoid space—both spinal and intracranial—and also has free access to the entire ventricular system. Reichert³ (1937) introduced air as a contrast medium in order to avoid the huge masses of lipiodol. With good roentgenograms and excellent interpretation of the air shadows, the results were almost as satisfactory. The most important advance was attained through a statistical study of these lesions. Simultaneously, and with identical results, and appearing in the same issue of the *Archives of Surgery* (1940), Love⁴ and Spurling⁵ found that 96 per cent of all spinal ruptured disks were situated at the fourth and fifth lumbar vertebrae. And if only lumbar disks were considered, over 98 per cent were in these two situations. This at once simplified the localization of the lesion to one of almost absolute precision, and entirely eliminated the need of spinal contrast media for its *localization*. However, this fact did not alter the need for a means of *diagnosing* the lesion. Semmes⁶ (1939), emphasizing the characteristic clinical picture of ruptured disks, suggested that no spinal injections were necessary. He reported 16 consecutive cases operated upon without contrast media or other tests, and at operation found disks in all cases.

Three important advances have improved upon, and greatly simplified, the operative treatment. Originally, a bilateral laminectomy was performed and the disk removed intradurally. (1) Mixter and Barr (1934) removed the

* Read before the Southern Surgical Association, Pinehurst, N C, December 9-11, 1941

RUPTURED INTERVERTEBRAL DISKS

disks extradiurally, but still used the bilateral approach (2) Semmes (1939), and shortly afterwards Love⁷ (1939), reported their removal by hemilaminectomy and by removing only a notch of bone in a lamina, and, finally, (3) Love⁴ (1940) removed a high percentage of ruptured disks through the interlaminar space without removing any bone whatever. Love's procedure is the acme of perfection, but can be accomplished only when the variable space between the laminae is of sufficient size. Practically, it does not matter whether a small bite of a lamina is removed for better exposure. In a recent case I removed a ruptured disk without sacrificing any bone whatever, but also without removing the ligamentum flavum. This, however, is probably of no practical import

CONCEALED VERTEBRAL DISKS

In a recent publication⁸ the writer disclosed a variation of this lesion which was called a "concealed disk," and which represents about one-fourth of the total number. Symptomatically, there was no difference whatever in the subjective or objective manifestations, but at operation the detection of the lesion was much more difficult. The end-results in treatment were precisely the same. A concealed disk is one that protrudes so slightly that it could hardly be found at operation unless one explored the subdural region with great care, but at the same time the findings are just as definite and unequivocal as the large protruding disks. Always, there is a very tiny bulge of the intervertebral space, with thickening of the spinal ligament, it indents with pressure of the forceps, and gives a sense of fluctuation to the pressure by them. And when incised, the forceps dip deeply into a cavity in the disk. When a curette is introduced macerated vertebral disk is obtainable. In none, however, does a sizable sequestrum of cartilage extrude through the opening. At times the concealed disk is laterally placed, at other times, at or near the midline. In every case the emerging nerve has been quite adherent to it, and this attachment is, I think, responsible for the pain, perhaps an intermittent protrusion of the disk may be a factor, but there is no proof of this, and the seemingly inelastic nature of the ligamentous capsule would appear to deny it.

There are always two component parts of a ruptured disk that are responsible for the patient's symptoms. (1) The necrotic interior of the disk, under pressure from edema, causes the backache, and (2) the protrusion upon, or adherence to, the emerging spinal nerve causes the sciatica.

The realization of these two elements is necessary for the certainty of a cure. A large protruding disk may be withdrawn and still not cure the symptoms. It is all-important that the interior of the disk be opened. It is not necessary completely to remove the contents of the ruptured disk to produce a cure—that is in fact impossible—but it is necessary to open it as widely as possible in order that the nonviable content, *i.e.*, the sequestrum, may be subsequently extruded through this opening. The principle in treatment is not unlike that of an abscess although the fundamental pathology is in no wise similar. There is no infective basis for an intervertebral disk. Always, it is a traumatic after-effect, and curiously, the trauma is always relatively slight

Curiously, a severe traumatic rupture of the spine never causes a protruding disk. The explanation is, I think, that with severe injuries the ligament over the dorsal surface is torn and provides the vent for its cure, much like that the surgeon produces by incising this ligament and opening the interior.

A ruptured vertebral disk is one of the most satisfactory lesions to treat surgically. When properly treated a cure can be expected in almost every case, and spontaneous cures, or treatment by braces, *etc.*, must be rare indeed. Recurring attacks are to be expected throughout life, or at least for many years. From the postoperative follow-up reports in the literature there have been 5 per cent recurrences. So far, I have not had a recurrence. This may be just a fortunate series, but I am inclined to believe that the explanation of recurrences is the failure to open the cavity in the body of the disk. Cures may result almost immediately, or they may take several weeks or even months, the difference, I think, is due to the time required for the complete extrusion of the affected disk. Bony fusion has been recommended by some operators, but this is neither necessary nor advisable. Patients should perhaps wear a brace for three months after operation, and should avoid heavy lifting and back strains during this time, thereafter they may continue in any occupation.

The diagnosis of ruptured intervertebral disks is now one of the greatest simplicity and accuracy from the symptoms alone. The characteristic story is (1) Low back pain, (2) spreading down the posterior aspect of one, or at times both legs, and (3) intensification of the pain in the back and leg by coughing or sneezing. The only item of importance in the examination is the reduction or loss of Achilles reflex on the affected side. At times there may be hypo-esthesia along the course of the affected nerve. Given this story, there can scarcely be any other lesion that need be considered. The pain begins after a heavy lift, a sudden twist of the spine, or an accident to the spine, or the trauma may even pass unnoticed. Movements of the spine intensify the pain. The pain is usually in recurring attacks, with more or less free intervals between, but the pain may be continuous, and in many cases it eventually becomes constant. With continuous pain, a psychoneurosis is a possibility, this and very occasional tumors (I have encountered one) are almost the only lesions that need be considered in differential diagnosis. At times the pain may be in the sacro-iliac region on one or both sides, occasionally there may be no back pain, and intensification of the pain by coughing and sneezing may be absent, but when present it leaves no doubt of the organic nature of the pain when a psychoneurosis is under consideration. The presence of normal Achilles reflex means nothing, the reduction or absence means a great deal, its loss may be referable to either the fourth or fifth disk.

Another anatomic factor must be borne in mind, namely, the not infrequent occurrence of a sixth lumbar vertebra, and when present the ruptured disk will probably be at the sixth disk. Two of our cases, in this recent series, occurred in this position, it was only at the operation that the sixth vertebra was recognized and subsequently checked roentgenologically.

RUPTURED INTERVERTEBRAL DISKS

I am particularly anxious to emphasize the purely clinical diagnosis, and to deprecate the use of all contrast media in the spinal canal, even to avoid spinal punctures. In the first place, these procedures are not necessary, they add nothing but the actual visualization of a lesion that is perfectly well known. They are painful procedures, and no one would desire a permanent deposit of lipiodol in the central nervous system. It is true that much of

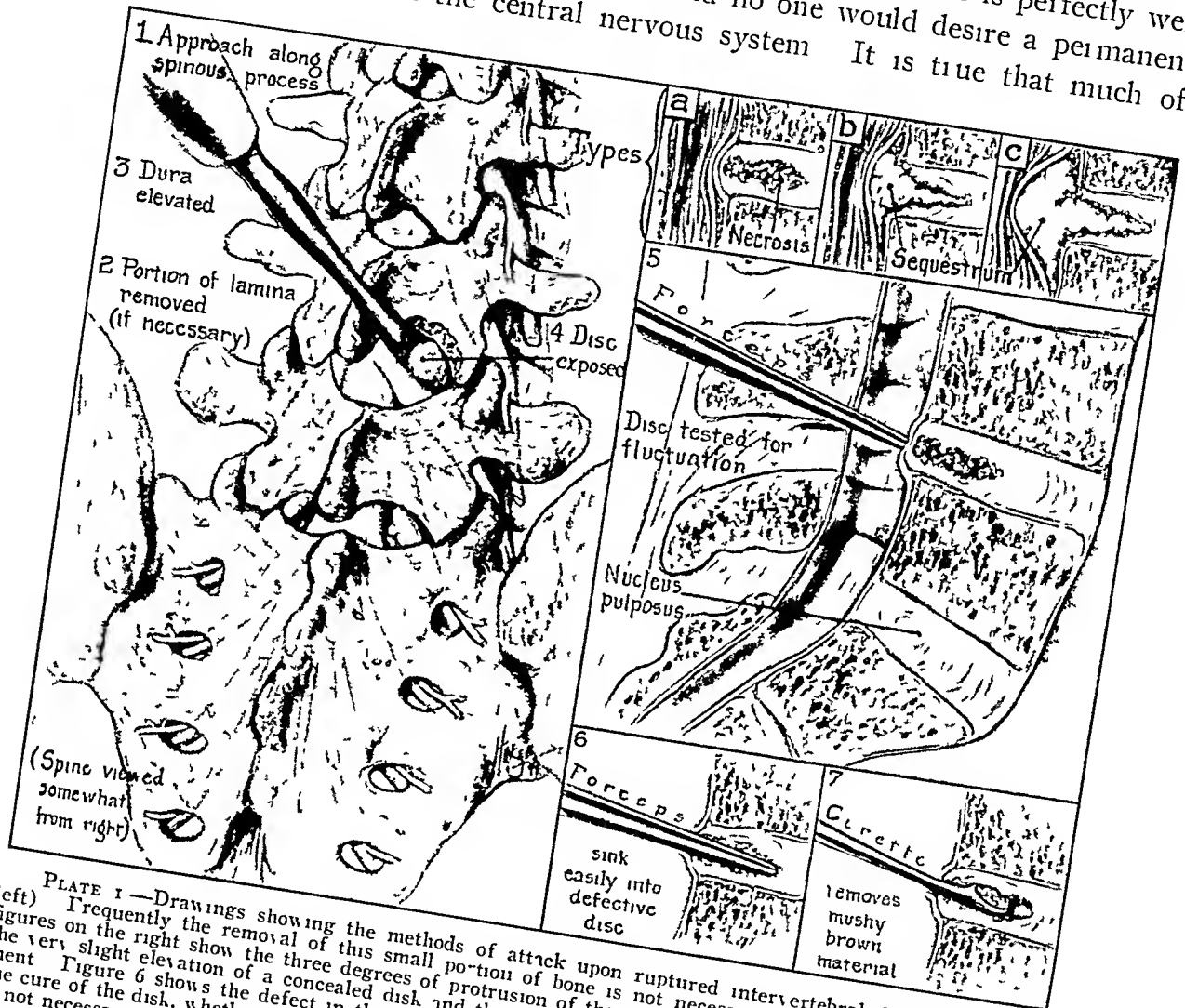


PLATE I—Drawings showing the methods of attack upon ruptured intervertebral disks (figure on left). Frequently the removal of this small portion of bone is not necessary (Love's procedure). The figures on the right show the three degrees of protrusion of the vertebral disk (a, b, c). Figure 5 shows the very slight elevation of a concealed disk and the indentation by pressure on the posterior spinal ligament. Figure 6 shows the defect in the disk itself. It is the wide opening of this that is necessary for the cure of the disk, whether of the protruding or concealed types. Curettement of the interior of the disk is not necessary, but in the concealed type one may obtain necrotic cartilaginous remains from the cavity. I see no reason to believe that the nucleus pulposus has any relationship to this lesion which involves much of the interior of the disk.

the lipiodol may now be removed at the time of operation, or when operation is not performed, by another puncture and aspiration, but the latter may be only partially successful and is, again, very painful.

The most important reason, however, for avoiding spinal contrast media is that the results are frequently negative when an actual ruptured disk is present. It is here that the "concealed disks" are all-important. None of them can possibly show a filling defect in either the air or lipiodol shadows, and concealed disks are more than 25 per cent of the total number. If lipiodol is used, and is negative, it means that these patients are excluded from the operative treatment that is essential for a cure, and without lipiodol

they are diagnosed with ease and certainty solely by analyzing the patient's symptoms

It is the recognition of the concealed disk that has completed the solution of this problem which approaches 100 per cent in accuracy of diagnosis. Before they were known there was a corresponding percentage of negative explorations, or, if lipiodol was used, a similar percentage of patients who were denied operation.

Since the elimination of contrast media, we have had (since April 1, 1941 to the time of this presentation, December 10, 1941) by clinical examinations alone, 63 cases without a single mistaken diagnosis. Lipiodol and air injections into the spinal canal, therefore, do far more harm than good, and their avoidance is most enthusiastically welcomed by the patient. In view of the fact that 96 per cent of all vertebral disks are at the fourth, fifth (and sixth) lumbar spaces (the percentage of the lumbar disks that are at these spaces is even greater), and since the unilateral approach is adequate to disclose the disk, regardless of the interspace involved, it only remains to make the diagnosis of a lumbar vertebral disk, and this is almost pathognomonic from signs and symptoms alone.

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DISCUSSION—DR CHALMERS H. MOORE (Birmingham, Ala.) The story of the extruded disk constitutes an important chapter in the history of surgery for relief of pain. After Dandy first reported this condition, in the late nineteen-twenties, interest in the subject lay dormant for several years. Recently, however, the literature has contained many references to the condition. There is no doubt that the disk accounts for much of what was formerly erroneously called sciatica. I am familiar with a series of 200 cases which fall into two groups, one in which compensation was a factor, and the other, in which compensation was not a factor. In the first group, 85 per cent of the results were poor, the patient still complaining of his preoperative pain. Whereas in the noncompensation group, over 90 per cent experienced relief.

This percentage runs about the same in my own series of 32 cases. Therefore, this compensation factor, present in so many cases, particularly in an industrial region such as Birmingham, must be borne in mind in evaluating results in this condition, which is now being recognized with such increasing frequency.

DR GEORGE E. BENNETT (Baltimore, Md.) It is a great pleasure for me to have the opportunity to say a few words about Doctor Dandy's discussion on intervertebral disks, and particularly in regard to diagnosis and treatment. The orthopedists have often referred to sciatica as a "headache." There is no bone or joint lesion which gives us more concern. Needless to say, we are all pleased that another etiologic factor has been definitely proven a cause of low back pain and sciatica.

I, fortunately, have lived long enough to have seen many cures developed for sciatica and low back pain. When I joined Doctor Baer, in 1910, he was manipulating a great number of patients for low back pain and sciatica, feeling that there was probably some displacement of the sacrum or the sacro-iliac joints. In 1914, we checked over approximately 200 of these cases and found that 40 per cent of them were cures. We were able to differentiate, and practically predict, the type of case that would be relieved by manipulation. It is a procedure that we use at present but we do not use it as indiscriminately as we did 25 years ago.

The next procedure that came into prominence was arthrodesis of the sacro-iliac joint for low back pain and sciatica. This is a procedure which is effective when one has a definite lesion of the sacro-iliac joint which is responsible for the pain and, in well selected cases, a high percentage of excellent results is obtained.

Next in order came the fusion of the lumbosacral articulation for the supposed slipping of a facet in an unstable spine, with local and referred pain. I can recall a very prominent orthopedic surgeon making the statement, some 15 years ago, that this was a cure for sciatica. This is a procedure which offers a very high percentage of very satisfactory results in those cases which are the result of abnormalities, *etc.*, which one sees about the fifth lumbar vertebra and the top of the sacrum.

In more recent years, Freiberg called attention to the fact that the pyriformis muscle in certain selected cases was the cause of sciatic pain. When one sees a patient with a definite pyriformis syndrome it is just as rational to divide the tendinous insertion of the pyriformis muscle as it is to operate upon the scalenus anticus for referred pain to the arm. There is a definite place for this operation but it is not the cure for all cases of sciatica.

Doctor Ober has also recently called attention to the shortening of the tensor fascia lata and advised division of this as a cure for sciatica. Only a few years ago, at a meeting of this same organization, a paper was read on this subject and many cures were reported. Again, this is a procedure which works very satisfactorily in the type of sciatica which is caused by shortening of the tensor fascia.

I think Doctor Dandy's observation of many years ago that cartilaginous injuries would produce sciatic pain is a great contribution, and that he and other neurosurgeons who have developed this field are to be congratulated. They have added one more definitely proven pathologic process which is productive of low back pain and sciatica, but I do believe that a careful, differential diagnosis is very essential before operation is recommended, and that it is not a procedure that should be used indiscriminately.

DR JOSEPH E J KING (New York, N Y) I want to say first that I agree with everything Doctor Bennett stated I was very glad that Doctor Mixter's name was mentioned, as I do not think the question of herniation of the disk should be discussed without mentioning the names of both Doctors Mixter and Alfred S Taylor It is to Doctor Taylor we are indebted for the hemilaminectomy, and inasmuch as most of the disks occur in the lumbar and cervical regions, the hemilaminectomy popularized by Doctor Taylor suffices

I have had very little help from the use of an, and have almost come to the conclusions reached by Doctor Dandy, namely, operation without any contrast medium On the other hand, it is very convincing to see the deformity in the lipiodol column produced by the disk However, once lipiodol has been instilled in the subarachnoid space, it should be removed, inasmuch as it "beads" around the component parts of the cauda equina if not removed I have seen this condition in three instances I understand the major portion of the lipiodol can be removed by aspiration through a rather large lumbar puncture needle, with the patient lying on the abdomen This has been demonstrated by the men in Boston

I was glad to hear Doctor Bennett emphasize the fact that all low back pains are not produced by herniation of an intervertebral disk In fact, only a small percentage of patients suffering from low back pain have herniated disks There is a tendency to ascribe too many instances of low back pain to herniation of the disk Several years ago it was the fad to believe that fusion was indicated in most cases of low back pain Today one notices the tendency to attribute many instances of low back pain to herniation of a disk

A number of writers have stated that hypertrophy or thickening of the ligamentum flavum may be present with or without a disk and may produce low back pain I should like to ask Doctor Dandy his opinion on this question

DR WALTER E DANDY (Baltimore, Md, closing) I shall only answer Doctor King's question about the ligamentum flavum My friend Doctor Reichert, of San Francisco, described it, but I have never been convinced that a thickened ligamentum flavum can cause sciatica or low back pain

Doctor Moore spoke of the functional disturbances simulating a ruptured vertebral disk This is very important One has to be on guard against the constant backache that always obtains in cases of malingering The ruptured intervertebral disk causes recurring backaches and recurrence after slight trauma This leaves no doubt about its organic nature They may, indeed, malingere afterward, but the evidence should be clear

GASTRIC ULCER, CARCINOMATOUS ULCER OR ULCERATING CARCINOMA? *

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IT WOULD SEEM TRITE to state that the therapy of any gastric lesion should be based on the pathologic nature of the lesion, on the recognition of the various mechanisms by which healing of the lesion is accomplished, and, when removal of the lesion is indicated, on the changing physiologic and chemical changes set up as a result of the surgical procedure employed to prevent recurrent ulceration. That certain benign gastric ulcers will heal under nonsurgical therapy properly carried out is well known. That such a group, however, cannot be so readily dismissed from our consideration as surgeons is evidenced by the fact that many such ulcers, even though benign in character, do not completely heal, but only seem to do so, and recur when the methods directed toward their treatment are discarded and the previous habits of eating and conduct of life are resumed. If such a cycle was confined only to those lesions suspected of being benign gastric ulcers, the seriousness of such lesions might be overestimated. That such is not the case, however, is evidenced by the fact that the same methods of evaluation which would seem to indicate healing of the lesion may also take place when the ulcer is cancerous, and an attempt to treat the lesion by nonsurgical methods when it reappears may delay surgical treatment until the lesion becomes inoperable. It is apparent, therefore, that one of our problems as diagnosticians and surgeons lies in trying to determine the pathologic nature of the lesion from the patient's history and physical examination and the reports of the roentgenologist and the gastroscoapist. In many cases this is exceedingly difficult. Although the expert roentgenologist may recognize the presence of a gastric lesion in 98 per cent of cases in which it is present, he has emphasized repeatedly that there is a definite percentage of error in distinguishing a non-malignant from a malignant gastric ulcer. This has too frequently been forgotten.

In a study of all of the patients operated upon for carcinoma of the stomach, between the years 1907 and 1938, inclusive, at the Mayo Clinic,^{18, 21, 22, 23} although the roentgenologist recognized the presence of a gastric lesion in 99 per cent of the cases, an unqualified diagnosis of cancer of the stomach was made in only 75 per cent of the cases in which gastric resection was performed. A roentgenographic report of gastric ulcer was made in 10 per cent of the cases. The gastroscoapist has aided us in recognizing the presence of lesions difficult to visualize roentgenographically, namely, those on the posterior cardiac portion of the stomach and some of those on the lesser curvature producing disturbances of motility suggesting that the lesion was duodenal.

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owing to the associated pylorospasm. Even when the lesion is observable, the possibility of misinterpretation of the pathologic nature of the ulcerating lesion by the gastroscopist must be definitely emphasized as a possible source of error. It is because of these difficulties in making a differential diagnosis between benign and malignant gastric ulcers and because many of them do not reach the surgeon until they have become large ulcerating carcinomata or perhaps until metastasis has occurred, that I have thought it worth while to call attention to some of the other possible sources of error which confront us all in differentiating between the benign and malignant gastric ulcer.

In the annual oration for 1936, delivered before the Medical Society of London, Sir James Walton quoted Stewart's statistics, which are so important that I think they should be constantly kept in mind, especially since Sir James said that they are generally accepted. Stewart stated that 10 per cent of chronic gastric ulcers become carcinomatous, that 17 per cent of gastric carcinomata originate in chronic gastric ulcers, but the incidence is probably much higher since many ulcerating gastric lesions are so large, when examined pathologically, that it is difficult to determine whether or not they might or might not have originated in a gastric ulcer. According to Katsch,⁷ 20 per cent of gastric ulcers become malignant, and Finsterei⁴ found that the ulcer was carcinomatous in 141 of 532 cases in which resection had been performed for gastric ulcer, an incidence of "20.9 per cent." Recent studies in this country by Allen and Welch¹ revealed that cancer was present in 14 per cent of cases in which an original diagnosis of ulcer had been made. In a series of cases reported by Klingenstein⁹ and Colp,² this incidence was 12 per cent.

Several years ago it was suggested that a therapeutic test could be made by subjecting patients who were thought to have benign gastric ulcers to a course of nonsurgical therapy, which consisted, for the most part, of neutralization of the gastric acidity, and of relief of pylorospasm and hypermotility of the stomach by complete rest and relaxation. Surgeons know the details of the nonsurgical methods directed to this end. It was thought that, if the symptoms subsided, the lesion disappeared in the roentgenogram, and blood disappeared from the stools, the ulcer was benign and it had probably healed. Experience has shown that these criteria of benignancy or even of healing have not stood the test of time, not only because many of the ulcers recurred as soon as the patient's dietary and physical restrictions, imposed during his stay in the hospital and during the ambulatory period, were discarded when the patient returned to work but because in a definite percentage of the cases the ulcers were carcinomatous. The recurrence of a chronic gastric ulcer treated by medical methods is quite understandable in view of the fact that unless complete control of gastric acidity can constantly be maintained, unless the associated gastrosplasm or pylorospasm can be constantly prevented, and unless something unusual happens to that unknown condition called "tissue susceptibility" to recurring ulceration, and with the same acid factors present as existed before the medical treatment was instituted, recurrence of the lesion takes place.

Three weeks ago I sent a patient into the hospital for a three weeks' trial of medical treatment. Examination revealed a gastric ulcer high on the lesser curvature of the stomach. After being in the hospital for a week symptoms attributable to the ulcer completely disappeared and tests for blood in the stools were negative. At the end of the third week, roentgenologic examination indicated that the lesion had disappeared, but gastroscopic examination revealed that an ulcerating lesion still was present. In other words, had a gastroscopic examination not been performed the erroneous impression might have been reached that the ulcer had healed. On the other hand, I recently operated upon a patient in whom a malignant lesion of the stomach had been suspected, but roentgenologic examination, on two occasions, at the clinic failed to reveal the presence of a gastric lesion. Gastroscopic examination, on the other hand, apparently revealed an ulcerating lesion high on the posterior wall of the stomach just off the lesser curvature. At operation, both extra-gastric and intragastric exploration, under visual control, disclosed only a hypertrophic gastritis with some spotty, grayish exudate here and there between the hypertrophied gastric rugae. Although these cases are exceptions, both of them were observed in the course of one month. They indicate that one cannot always rely too much on the roentgenogram in determining the changing character of a gastric ulcer, likewise, the gastroscopist's interpretation of his findings is subject to the same possibility of human error. To emphasize the point further, I should like to mention another case in which roentgenologic examination revealed a sizable crater due to a gastric ulcer. Twenty-four hours later, a roentgenologic examination made under similar circumstances revealed that the crater was only half as large as it had appeared to be on the previous day. Naturally, such a degree of healing probably did not take place in so short a time.

According to Schindler,¹⁵ the seeming disappearance, or the decrease in the size, of the crater when the lesion is malignant is due to the infiltration of the crater by the carcinomatous process originating in one edge of the ulcer, granulation tissue filling in the remainder.

At the present time, my colleagues, Priestley and Judd,* are studying a group of 170 cases, observed at the clinic between 1930 and 1937, in which a diagnosis of gastric ulcer was made and the patients were placed on a medical regimen. Many of these patients were operated upon later because of recurrence of the benign lesion and others for gastric carcinoma. Other similar studies of the permanency of supposed healing of chronic, benign gastric ulcer, when the patients have been placed on a medical regimen, should be carried out.

It may have seemed out of place to consider the so-called laboratory methods of determining the presence and the nature of ulcerating gastric lesions before considering the symptoms. I have done so purposely because I wish to emphasize the inconsistency of assuming that patients with benign ulcers of the stomach have symptoms which are characteristic of benignancy.

* Doctors Priestley and Judd will publish the results of their study when completed.

Such symptoms are frequently referred to as "the ulcer type of dyspepsia" and are characterized by burning epigastric pain that appears one to two hours after eating and is relieved by ingestion of food or bicarbonate of soda, or by emptying the stomach. These, according to Sippy, were more accurate in differentiating a benign and a malignant gastric lesion than the roentgenologic examination, as carried out at that time, 1919 and 1920, in his hospital. The fallacy of this viewpoint is evidenced by the fact that in 33 per cent of the cases of carcinoma of the stomach in which operation was performed at the clinic between 1907 and 1938, inclusive, the patients had an ulcer type of dyspepsia in almost a similar percentage of cases, this ulcer type of dyspepsia had been the first symptom which the patients had observed. Of even greater importance, it seems to me is the fact that in these cases medical treatment directed toward controlling the acidity and relieving gastrospasm was followed by effective relief of pain in 80.6 per cent of the cases. Several years ago I stated that it was my impression that 20 per cent of the patients upon whom I operated for carcinoma of the stomach had been treated medically for many months on the assumption, from their history, that a benign peptic ulcer was present and it was only when the patients had failed to obtain relief of symptoms by these measures that roentgenologic examination had been performed and revealed that the lesion was not a benign ulcer of the stomach or duodenum but a malignant lesion of the stomach. As a history suggestive of gastric ulcer is obtained in one-third of the cases in which operation is performed for cancer of the stomach, and since medical treatment produces symptomatic relief in 80 per cent of cases, it is quite apparent that the same difficulties in interpreting the pathologic nature of a gastric ulcer will be encountered.

In considering such a parallelism in symptoms of benign and malignant lesions of the stomach, one invariably wishes to know if a study of gastric acidity in such cases might not be helpful. The presence of achlorhydria in a case of ulcerating gastric lesion usually means that the lesion is malignant regardless of the roentgenographic report, but on the other hand a relative achlorhydria was present in only 51.4 per cent of the cases of gastric carcinoma in which resection was performed at the clinic and to which I have referred previously. In comparing the values for hydrochloric acid it was noted that in cases of both groups, namely, those in which resection was performed as well as those in which palliative procedures were carried out, free hydrochloric acid was present and that the values, as determined by the method of Topfer, ranged from one to 29 in approximately 30 per cent, from 30 to 49 in approximately 15 per cent, and 50 degrees or more in approximately 5 per cent of the cases, respectively. Allen and Welch¹ found that "the percentage of cases with free acid in the stomach is just as high with 'ulcer-cancer' as it is with benign ulcer."

There are other factors responsible for the patient not being given the benefit of surgical removal of a chronic gastric lesion at an early stage, among which is the opinion of some internists that the risk of removal of a gastric ulcer is greater than the possibility of the lesion being malignant. With this

I wish to take definite issue, for the risk associated with removal of gastric ulcer should not exceed a maximum of 5 per cent, and it is possible to operate upon a large series of patients who have gastric ulcer and achieve a mortality rate of considerably less than 5 per cent. In point of fact, partial gastrectomy was performed at the clinic in 89 cases in 1939,¹³ with a mortality rate of 2.2 per cent, and in 88 cases in 1940,⁶ with but one death. In addition, excision of the ulcer, gastro-enterostomy, or both procedures were performed in 17 cases of gastric ulcer, with no deaths. Operation was performed in 64 per cent of cases of gastric ulcer observed in 1939, and in 61 per cent of the cases observed in 1940.*

In cases in which operation was performed for gastric ulcer, patients were selected carefully; many underwent a period of observation and a therapeutic trial of nonsurgical treatment in the hospital, and some were allowed to return home for two or three months during which time an ambulatory regimen was carried out. At the end of such a period, reexamination was carried out. Partial gastrectomy was performed only when the nature of the lesion and the condition of the patient warranted this procedure. From the standpoint of the possibility of recurrence of ulceration, I have never seen a benign gastric ulcer recur or a gastrojejunal ulcer develop after partial gastrectomy when half or more of the stomach (which includes the ulcer) was removed. This has not always been the case, however, when the gastric ulcer was excised and gastro-enterostomy performed. On the other hand, in the nonsurgical methods of treatment, recurrence takes place in a definite percentage of cases.

Another argument sometimes used in a persuasive fashion is that when the lesion is situated high on the lesser curvature, according to the roentgenologic examination, not only a course of medical therapy but a continuation of medical therapy is indicated because of the relative inaccessibility to surgical removal and hence the increased surgical risk.

In a paper dealing with caudal gastric ulcers, Cleveland and I^{17, 20} emphasized that in several cases gastric ulcers which appeared, on roentgenologic examination, to be situated very high on the lesser curvature were really not as inaccessible as they seemed to be, for, at operation, it was found that the perforation of the lesion into the capsule of the pancreas had so shortened the stomach remaining above the lesion as to give an erroneous idea of the amount of stomach between the ulcer and the esophagus. In these cases there was actually more uninvolved stomach than the roentgenograms indicated. The early division of the gastrohepatic omentum at a very high level assists in mobilizing the upper part of the stomach so that unusually high lesions could be removed without too great difficulty, especially when the original method of Billroth or the Hofmeister modifications of the Polya operation are employed, and when one removes a greater portion of the lesser curvature (containing the ulcer) than of the body or greater curvature.

* This percentage of patients operated upon for gastric ulcer should be compared with 18 per cent of patients with duodenal ulcer who were operated upon in 1939, and 15 per cent operated upon in 1940.

To confirm the impression that although removal of gastric ulcer is made more difficult when the lesion is situated above the incisura angularis but the mortality rate from the operation is not increased appreciably, Cleveland and I^{17 20} studied 42 consecutive cases in which operation for a benign lesion situated in the cardial region of the stomach was performed at the clinic in 1938 and 1939. The mortality rate in these cases was 2.3 per cent. Thirty-five of the patients had benign ulcers in the cardial portion of the stomach. In 26 of the cases, partial gastrectomy was performed, with one death, a mortality rate of 3.8 per cent. In four cases, the ulcer was excised and gastro-enterostomy performed. In one case, excision of the ulcer alone was undertaken, and in four cases, gastro-enterostomy was performed. In the nine cases, in which surgical procedures other than partial gastrectomy were employed, there were no deaths. The relative incidence of lesions in the cardial portion of the stomach in these two years was 14 per cent in the 542 cases in which operation was performed for lesions of the stomach. These included both cases of benign and malignant lesions.

Finsteier⁵ and Rieder¹⁴ both reported with favor on high gastric resection and removal of the ulcer whenever possible, and both advised the Kelling-Madlener type of subtotal gastrectomy, which allows the ulcer to remain *in situ* when it is situated too high to be removed with safety. They postulated that, by removal of the greatest acid-forming portion of the stomach, more permanent cure is effected. In this procedure, which was originally proposed by Kelling⁸ in 1918, and was described and brought into favor by Madlener¹¹ in 1923 and 1929, resection of the stomach below the site of the ulcer is accomplished by anastomosis of the stomach to the duodenum by the Billroth I-type of procedure. Finsteier⁵ has reported anastomosis of the end of the stomach to the side of the jejunum, posterior to the colon, in the palliative resection when fixation of the duodenum might cause tension on the suture line. Lewisohn¹⁰ said that he did not favor the Madlener procedure, as the postoperative results of Madlener's operation in a large number of cases are unsatisfactory, the ulcer is not put at rest and gastric acidity is seldom sufficiently high preoperatively to require gastric resection for its reduction.

I have found the procedure of choice to be subtotal gastrectomy, in which the incision is carried well beyond the lesion, which is removed. The advantages of this procedure are as follows: (1) Removal of the lesion with its possibilities of hemorrhage, perforation or malignant degeneration, (2) relief of associated pylorospasm, and (3) decrease in the quantity of and concentration of hydrochloric acid secreted and stimulated which results in an almost constant incidence of relative achlorhydria with almost total absence of gastro-jejunal ulceration. The Polya-type of end-to-side anastomosis posterior to the colon, without entero-anastomosis, is, in my opinion, preferable to anterior anastomosis.

The Billroth I (Habeier) method of direct anastomosis as modified by Horsley and Haberer is occasionally employed in selected cases and is an excellent procedure in certain cases of gastric ulcer and carcinoma. It is par-

ticulaily useful in instances in which the duodenum is mobile and the lesion is in the lower third or half of the stomach, for, under these circumstances, the end-to-end anastomosis can be made without tension on the suture line. It was noted by Clagett and me,¹⁹ in a study of 272 consecutive operations for gastric ulcer performed at the clinic, from January 1, 1933 to January 1, 1937, that this procedure was employed 22 times in contrast to the posterior Pólya operation, which was employed 131 times. It should be emphasized that the results of the Billroth I procedure for gastric ulcer are satisfactory in a much higher percentage of cases than are operations of a similar type for duodenal ulcer. This is probably due in part to the fact that the Billroth I operation produces a relatively higher incidence of postoperative achlorhydria in cases of gastric ulcer than it does in cases of duodenal ulcer.

When the condition of the patient is such that removal of the lesion as a part of subtotal gastrectomy cannot be undertaken without too great risk, then as safe a procedure as possible should be utilized which sufficiently reduces gastric acidity and reduces gastrospasm so that healing of ulceration may be anticipated. Surprisingly good results may be obtained by less radical methods, such as excision of the ulcer with gastro-enterostomy or occasionally by only excision of the ulcer. Protection against further ulceration is accomplished by reduction of gastric acidity by the gastro-enterostomy. This was done 50 times with very good results in the series of cases studied by Clagett and me. Eusterman and Balfour³ showed that 79 per cent of 100 patients upon whom gastro-enterostomy had been performed for gastric ulcer were well after five years. This procedure, which carries a low risk (a mortality rate of 3.9 per cent in 540 cases, according to Eusterman and Balfour), is thus worthy of consideration when conditions make excision or resection impossible. The palliative resection of Madlener, in which the ulcer is also left behind, has not been utilized at the clinic.

Excision with knife or cautery may occasionally be done without gastro-enterostomy but it is not recommended because it does not offer an alteration in gastric function to prevent recurrence*. In the occasional case it has been utilized with good results. It does enable microscopic study of the lesion. Similarly, segmental or sleeve resection may be done to remove the lesion, but disturbance in gastric peristalsis may follow in its wake even to the extent of the development of an hourglass deformity owing to contracture at the site of the anastomosis. In addition, little change in gastric function results, and recurrent ulceration may occur. It has been used with some success in selected cases, however, but not in recent years.

It is to be repeatedly emphasized that, when possible, removal of the lesion in some manner should be done to enable microscopic examination of the lesion. If an excision of the ulcer is done and the lesion should prove, on microscopic examination, to be malignant, its removal by partial gastrectomy gives the patient the best chance of cure, for partial gastrectomy not only removes the lower portion of the stomach beyond the point where direct ex-

* Reduction of gastric acidity and relief of pylorospasm

tension occurs (duodenal side of the pylorus) but it removes the lymphatic region in the adjacent gastrocolic and gastrohepatic omenta, which might harbor malignant cells extending from the primary lesion. No one, by choice, desires to leave behind a gastric ulcer with the menace of malignancy in it, but, if survival of the patient is deemed impossible with its removal, some less satisfactory procedure must be undertaken.

SUMMARY

The treatment of gastric ulcers should depend on the pathologic nature of the lesion, remembering that a definite incidence, 10 to 20 per cent, of carcinomatous ulcers cannot be distinguished roentgenographically from benign gastric ulcers, and that there is not a definite symptom complex pathognomonic of benign ulceration of the stomach, for in one-third of the cases in which operation was performed for gastric carcinoma the patients had ulcer-like histories and four-fifths of these patients obtained temporary relief of symptoms when placed on a nonsurgical medical regimen. Experience has shown that a therapeutic trial of medical treatment during which the ulcer seems to disappear roentgenographically, symptoms subside, and blood disappears from the stools, cannot be relied on either to exclude the possibility of the lesion being malignant or as an indication that recurrence of the benign ulceration will not take place when the patient returns to his usual habits and activities of life.

In the past few years operation has been performed in approximately 60 to 64 per cent of the cases of gastric ulcer observed at the clinic, and the mortality rates have not been greater, and sometimes have been less, than for operations of similar type performed for duodenal ulcer. During the same period, the incidence of patients operated upon for duodenal ulcer varied from 15 to 18 per cent. The results of surgical treatment of benign gastric ulceration when subtotal gastrectomy is performed are well-nigh perfect—superior to similar operations for duodenal ulcer. To date, I have not seen a case of recurrent benign ulceration in which half or more of the stomach was removed with the benign gastric ulcer.

Efforts should be directed to determine accurately the percentage of patients with benign gastric ulcers who have remained well without recurrence after a course of nonsurgical treatment.

Although subtotal gastric resection is the operation of choice and should be employed preferably in all cases of gastric ulcer, there is a place for the less radical procedure of excision of the ulcer and gastro-enterostomy or gastro-enterostomy alone. Ulceration has recurred rarely in some cases in which excision and gastro-enterostomy have been performed but more frequently when excision of the ulcer only was performed.

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GASTRIC RESECTION FOR DUODENAL ULCER *

FOLLOW-UP STUDIES

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AMERICAN SURGEONS have approached the problems of radical operative procedures for duodenal ulcer in a cautious manner. This is the natural attitude since only a small percentage of all patients with duodenal ulcer fail to respond to the conservative measures carried out by our medical colleagues. Actually, it appears that a large percentage of the satisfactory results from gastrojejunostomy or pyloroplasty were in those patients who might have avoided surgery entirely. Since there are so few individuals who cannot be adequately treated medically, it has taken some years to realize that in this small group of patients with intractable ulcer, palliative operations are associated with a high percentage of failures.

It is difficult to take the attitude concerning the stomach that we have long since accepted for hyperactive endocrine glands. Since, as yet, we have not been successful in finding a more satisfactory solution to the problem of many types of pathologic physiology, it remains necessary, at the moment, to relieve these conditions by radical surgery. In the case of duodenal ulcer, we are dealing with a poorly understood disarrangement of normal physiology. Hyperacidity, tissue susceptibility, psychologic disorders and various other factors of temperament, environment, and economics play a rôle. Doubtless, in some instances, the location of the ulcer makes it unlike the majority of such cases in regard to nature's ability to heal the lesion, and, if healed under ideal conditions, it is prone to recur, even in spite of adequate guidance by the physician and cooperation on the part of the patient. Thus, we have the problem of protecting such individuals from repeated or continuous disability, from episodes of massive hemorrhage and from repeated perforation. This group, as a whole, comprises approximately 20 per cent of all duodenal ulcer patients coming to a large urban hospital. Of these, about one-fourth are operated upon for acute perforation and this complication will not be discussed in this presentation. Of the remaining 15 per cent, more than one-third are subjected to surgery because of cicatricial obstruction due to ulcer of long standing. The remaining cases, representing less than 10 per cent of all duodenal ulcers, are turned over to the surgeon because of massive hemorrhage or intractability. It is with these last two groups that we particularly wish to deal in this paper, since they are almost as resistant to palliative operations as they are to medical therapy.

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Gradually, there has come about a more radical attitude regarding the kind of surgery indicated in this small group of recalcitrant cases. Many European surgeons have advocated resection of one-half or more of the distal stomach for duodenal ulcer for 20 or more years. In America, there has been a hesitancy to adopt these radical principles although some men, notably Beig¹ and Lewisohn,² advocated and practiced these methods several years ago. It was necessary first to improve surgical principles to such a degree that the mortality for a radical operation would not be sufficiently high to offset the better results that might be obtained. Perhaps more importance was placed on the actual accumulation of experience to demonstrate that the mortality could be low and the late results better than those following less radical measures. It was hard for us to forget that approximately 80 per cent of duodenal ulcer patients were relieved by palliative surgery in the days when such a procedure was the accepted treatment. Finally, we realized that in this large group of patients responding to short-circuit operations, there were many who would have done very well on a medical regimen. Eliminating the usual type of ulcer patient, we are presented with an entirely different problem and it is these unyielding cases that we must consider in a different light than the majority.

The first question which we must strive to settle concerns the results that may be expected from these radical operations. Most of the reports dealing with the subject are concerned only with the immediate operative mortality and the various modifications of the technic of the procedure. Walters and Cleveland,³ St John, Harvey, Gius and Goodman,⁴ and Roscoe Graham⁵ have made preliminary studies of late results. It is our intention to add our experience in this field, realizing fully that our cases are few in number and not of sufficient duration to consider them as end-results. It is obvious, however, that the trend of operation for duodenal ulcer in our hospital has definitely changed during the past ten years, so that now very few cases are operated upon by palliative methods. Doubtless, this is due to the fact that these less radical procedures are associated with a very high percentage of poor results. On the other hand, every patient who has had a radical resection of the distal half or more of the stomach and pylorus has been free of symptoms and none has as yet developed recurrent or anastomotic ulcers.

Analysis of 67 cases of jejunal (anastomotic) ulcers in our clinic indicates that one-third originate within the first year and two-thirds within the second year after the primary operation. Occasionally, this complication develops later and, in fact, two of our patients developed jejunal ulcers 18 years after their operation for duodenal ulcer. During the past ten years, 16 jejunal ulcers have been admitted following posterior gastro-enterostomy previously performed in this hospital, 22 others were admitted during the same period, who had had the gastro-enterostomy performed elsewhere. Since 137 patients survived posterior gastro-enterostomy in this decade, the incidence of jejunal ulcer is well over 10 per cent. This complication of stomal ulcer is by far the most serious that occurs, but there are other evidences of patients being

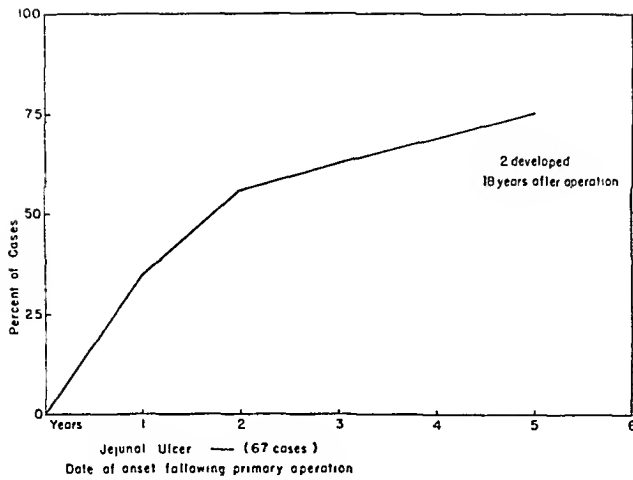


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unrelieved of symptoms or even in a worse state than existed prior to operation. Accepting the fact, then, that the poor results are so common in those having simple posterior gastro-enterostomy in this decade that we can eliminate this group from further discussion, we will concentrate on the results, so far known, from other types of operation.

TABLE I

DUODENAL ULCERS

Massachusetts General Hospital

ULCERS INTRACTABLE BECAUSE OF PAIN OR BLEEDING

	Type of Operation		
	P G E	Resection	Other Operations
1922-1926	87	6	14
1927-1931	37	8	6
1932-1936	20	39	7
1937-1940 (4 years)	8	65	5

It has gradually become obvious to us that the type of surgery most likely to succeed is gastric resection. The manner in which this has been performed and the amount of stomach sacrificed has varied somewhat. We have been influenced by the opinions of European surgeons as well as by our more radical American colleagues. There has now come about a general consensus of opinion that intractable duodenal ulcer should be treated by gastric resection. The ideal situation appears to be one that allows the safe removal of not less than one-half of the distal stomach and that portion of the duodenum containing the ulcer. By a process of long preparation, the majority of patients can be brought to the operating room with a lesion healed sufficiently to make such a procedure safe. Subtotal gastrectomy for duodenal ulcer is dangerous if the patient is depleted from recent hemorrhage or from partial obstruction, or has an acute lesion associated with extension of inflammation due to perforation into the pancreas and other neighboring

structures. We should be able to avoid the first two risks by adequate preparation, while in most instances the acute and subacute reactions can be allowed to subside before undertaking the operation. The chief danger in the latter group is the management of the duodenal stump. This has brought about methods of resection for exclusion of the ulcer area and without doubt these have lowered the risk in certain cases. The results, however, have not been so good and if the antial mucosa has been left, the results are as bad as if not worse than those obtained by gastro-enterostomy.

In the ideal operation, one is able to resect the pylorus and find sufficient healthy duodenum to secure an adequate inversion of the stump. We believe that this requires at least three-quarters of an inch of free duodenum. We have felt more secure with two rows of catgut sutures inverting the cut end of the duodenum so that its peritoneal coats were in contact with each other. We think that if this is done so that no mucosa protrudes between the suture lines, healing will be rapid and secure. A tab of omentum fixed over the stump is doubtless an added safeguard. If one has to be satisfied with sutures under tension, inadequate tissue of suitable healing properties or closure of the anterior wall of the duodenum to the pancreas over a remaining ulcer bed, then complications with prolonged convalescence and possible fatal outcome must be expected. With increased experience, the surgeon will find that he will be able to remove safely the diseased area in a larger percentage of cases. Dissection of the ulcer area first is not recommended since often this may be carried far enough to break up the inflammatory protection about the lesion, only to reveal the involvement of the biliary and pancreatic ducts. Having done this and then resorting to an exclusion type of resection leave the ulcer in a more likely state for perforation. We have had this experience with fatal perforation three days following a subtotal gastrectomy for acute massive hemorrhage. Reports are available of massive hemorrhage from the ulcer when treated in this manner, although, so far, it has not occurred in our cases. One can, however, look the situation over carefully and if there is reasonable hope that the ulcer area can be safely included in the resection, then the lateral border of the duodenum can be freed, as originally advocated by Finney⁶. Having done this, one may determine the course of the common bile duct and its point of entry into the duodenum. Frequently, one can be sure that the area involved in the ulcer is sufficiently proximal to this point to allow a safe removal.

If there is extensive involvement of the whole area, particularly if the lesion is fairly acute, then it is safer to elect some form of resection for exclusion. This term we owe to Finsterer,⁷ who at first described it as any resection proximal to the ulcer whether the distal segment included the pylorus or not. He found, after his first publication, that several other surgeons had tried similar procedures. In his first paper on the subject, he advised removal of the antial mucosa and turning in only the muscular and serous coats when this segment was utilized. When the duodenum was turned in

with the ulcer *in situ*, he later advised routine drainage of the area. In subsequent publications,⁸ he not only advised leaving the antral mucosa but felt that these cells were important to a good result. He stressed a massive resection of two-thirds to four-fifths of the stomach and attributed his lack of late jejunal ulcer to the large amount of stomach removed. We have, perhaps erroneously, not considered the resections beyond the pylorus but proximal to the ulcer as resections for exclusion, and have grouped them in the same category as true subtotal resections. The results in this small group would appear to be as good as a resection including the ulcer, but the postoperative complications were more numerous and the mortality was higher. This was due largely, we are sure, to the inadequate management of the duodenal stump. We have included as resections for exclusion only those cases that have been transected through the antrum. In this group, we have ten cases that did not have the antral mucosa removed, and five of the nine survivors developed anastomotic jejunal ulcers. The other four are so far symptomless, and we are sure that these did not have a more radical resection than those who developed jejunal ulcers. We have removed the mucosa in the antral segment in 13 resections for exclusion and have erroneously called this Bancroft's modification. We are indebted to Bancroft⁹ for the idea after his report on such a maneuver for the modification of the Devine operation. In these cases with a resection of more than half of the stomach, leaving the antrum but removing its mucosa, we have had one death in 13 cases. In those who survived the operation, there has been no single instance of anastomotic jejunal ulcer so far. Although this would indicate that the mucosa contained the elements needed to produce hyperacidity in the proximal stomach remnant, the group is so small that one can only use it for comparison with the other small group that did not have these cells eliminated. We regard this procedure as definitely second best on the basis of considerable increase in postoperative complications over those who could safely have the resection carried into healthy duodenum. Complications arose due to the thin, friable structure of the posterior wall of the antrum after removal of its mucosa. One must exercise care in the denudation and carefully infold the remaining tissues to close the dead space adequately. We have found it best not to ligate the mucosa at the pylorus but leave it open since this enhances the discharge of serum into the duodenum.

McKittrick¹⁰ has suggested a deliberate two-stage resection in poor risks and in patients who had extensive ulceration or inflammatory reaction. The relative smoothness of the immediate convalescence following resection for exclusion without interference with the ulcer or antral mucosa is apparent to those who have used it. Also, the ease with which this segment can be removed after weeks of physiologic rest is impressive. Doubtless, an occasional patient so treated will develop jejunal ulcer before the second stage can safely be undertaken. On the other hand, the majority of cases so treated will survive the two procedures and rarely will jejunal ulcer arise in the six to eight weeks' interval between them. In one instance, McKittrick

GASTRECTOMY FOR DUODENAL ULCER

has observed the healing of a jejunal ulcer after the simple removal of the pyloric segment. This patient had had three operations in other hospitals before coming to us. The last resection had left him with a very small proximal stomach segment but a very painful disabling anastomotic ulcer. Although it had been reported that he had had a true subtotal resection, on exploration it was found that a small antral segment had not been removed. The jejunal ulcer pain was immediately relieved after this pyloric segment was eliminated.

We have reoperated upon one man twice for jejunal ulcer after the first resection for exclusion without removal of the antral mucosa. The second operation, six months after the original, consisted of a higher resection of the stomach and the segment of jejunum containing the stoma and its ulcer. Less than two years later, anastomotic ulcer developed in spite of great care on the part of the patient. By this time, we were aware of the danger of the antral cells so that at the third operation the pyloric segment was removed as well as the second anastomosis with its ulcer. Although this man was nearly 70 years of age and somewhat arteriosclerotic, he had an easier convalescence following the third procedure than either of the other two. He has remained entirely symptom-free now 24 months after his last operation. We are convinced that the higher resection played a lesser rôle in the cure of these patients than did the elimination of their antral segment.

TABLE II
DUODENAL ULCER
Massachusetts General Hospital
MORTALITY (1931-1940)

	486 Operations	Died	Per Cent Mortality
Acute perforation	165	44	26.6
P.G.E.	151	14	9.3
Resection	151	14*	9.3
Other operations	19	2	10.5

* Seven patients died after operation for massive hemorrhage

TABLE III
DUODENAL ULCER
Massachusetts General Hospital
MORTALITY ACCORDING TO TYPE OF OPERATION (1931-1940)

	Cases	Deaths	Per Cent
Resections			
Subtotal	56	3	5.4
Partial (Pólya or Billroth-II)	42	6	14.3
Billroth-I	4	0	
Pylorotomy	26	3	11.5
Finsterer exclusion (through antrum)	10	1	10.0
Finsterer exclusion (plus removal of antral mucosa)	13	1	7.7
Gastrojejunostomy	151	14	9.3
Gastroduodenostomy	8	1	12.5
Pyloroplasty	10	1	10.0
Devine operation	1	0	

In Tables II and III, it is apparent that, in our hospital, gastric resection does not carry a higher mortality rate than less extensive operations. We have classified those patients having more than the distal half of their stomachs, including the pylorus, removed, as subtotal resections. Those that had a quarter to a half removed are designated as having partial gastrectomy, and those who had the pylorus only removed with gastrojejunal anastomosis as pylorotomies. The Billroth-I operation was rarely performed and was probably not more than a pylorotomy. We have described in the foregoing paragraphs our classification of the two resections for exclusion practiced in our institution. Simple posterior gastro-enterostomy carried the same mortality as all of the resections. In the former group, one may immediately expect that these were in the older, poorer risk patients, but this is not the case. In the latter group, we have included seven failures from resection during an episode of massive hemorrhage. All but two of these failures were in attempts to rescue a patient who had been bleeding for over a week. The recovery group includes six cases, all beyond the age of 50, who were operated upon within 72 hours of the onset of bleeding.

TABLE IV

DUODENAL ULCER

Massachusetts General Hospital

COMPLICATIONS FOLLOWING 151 GASTRIC RESECTIONS (1931-1940)

	Fatal	Nonfatal
Peritonitis	4	1
Pulmonary	3	13
Duodenal fistula	1	3
Section of common duct (bile peritonitis)	2	1
Hemorrhage	4	1
Obstruction	0	8
Miscellaneous	0	9

In Table IV, we have analyzed the complications following gastric resection for duodenal ulcer and grouped them as fatal or nonfatal. Those dying of peritonitis were due to the ulcer harboring virulent organisms. By preliminary culture of the stomach contents, and by the use of sulfonamides, one might hope to eliminate these deaths. Fatal pulmonary complications are much less common than in previous decades and when they occur, are usually in aged, debilitated patients. Duodenal fistula should be a rare complication if one uses the proper operation for each case. It is important to recognize leakage when it starts and immediately establish external suction drainage. One might occasionally benefit by drainage at the time of operation, using extreme care to avoid contact of the wick with the sutured duodenum. We were shocked to find that there were two common ducts injured during gastric resection for duodenal ulcer, with fatal bile peritonitis. Both of these were patients of the same operator. The nonfatal injury to the duct was recognized and repaired at the time of operation. This not only complicated the convalescence but the patient still has symptoms from a poorly functioning choledocho-enterostomy. Hemorrhage after resection should be

1211c One fatal instance was in a patient with a peculiar hemorrhagic diathesis. On reexploration, blood was found to be coming from every cut surface, including his abdominal wall. Although it was before synthetic vitamin K was available, his prothrombin level was determined immediately after operation and found to be 20 per cent of normal. It is interesting to note that postoperative hemorrhage may occur in patients of a normal prothrombin level, and we have had two similar episodes in other types of surgery. One woman following radical breast amputation and one man following subtotal thyroidectomy bled in the same manner. These both had normal prothrombin times and finally escaped bleeding to death after several transfusions.

Obstruction of the stoma,¹¹ although annoying, should rarely prove fatal. In depleted patients or those whose anatomic variations make early function of the stoma unlikely, a concomitant jejunostomy for feeding is a wise precaution (Clute¹²). Stomal obstruction should not be allowed to progress longer than one week on conservative management. Jejunostomy for feeding, undertaken in a logical manner before it is too late, will invariably allow the stoma to right itself, provided the first operation has been properly performed.

TABLE V
DUODENAL ULCERS
Massachusetts General Hospital
RESULTS ACCORDING TO TYPE OF OPERATION (1931-1938)

	Excellent	Good	Poor	Operative Deaths	Lost
Resections					
Subtotal	6	1		1	1
Partial	29	5	2	7	9
Pylorectomy	5	2	3	2	2
Finsterer exclusion (through antrum)	4		5	1	
Finsterer exclusion (plus removal of antral mucosa)	1				
Billroth-I	1		1		1
Gastroduodenostomy	2		2	1	2
Pyloroplasty	1		3	1	5
	—	—	—	—	—
Totals	49	8	16	13	20

The results on a small group of cases, followed from three to nine years, are classified in Table V. An excellent result signifies that the patient has remained symptom-free since operation, and able to do his regular work. Thirty-five of 43 patients (81 per cent) who had partial or subtotal resections are classified in this group. Although all of these patients are cautioned about the use of highly seasoned foods, alcohol, and tobacco, many of them gradually discard all precaution in this regard.

Good results signify a situation that, although not perfect, allows a patient to carry on his usual occupation but with some occasional discomfort, such as nausea after eating or epigastric distress and sour eructations. One patient has an annoying gastrocolic reflex, without evidence of jejunal ulcer or gastrojejunocolic fistula. Another patient had a single episode of massive bleeding five years after the distal half of his stomach and pylorus was re-

sected, with a posterior Polya anastomosis. The origin of the hemorrhage was proven by gastroscopy to be due to gastritis. This cleared up on conservative measures. Doubtless, this patient had become too confident regarding the operative cure and had abused his gastric mucosa unwisely.

The poor results represent nine proven and two suspected jejunal ulcers. One patient continued to have periodic hemorrhage and another had persistent pain. Three of the jejunal ulcers following the Finsteier exclusion operation have since been reoperated upon and relieved. The high incidence of stomal ulcer after the exclusion operation, without excision of antral mucous membrane, has also been emphasized by Fromme¹³ and Haberer¹⁴. One failure following pyloroplasty and one following gastroduodenostomy, with subsequent massive hemorrhages, should be reoperated upon. One patient who developed anastomotic ulcer eight months following a Billroth-I operation was subjected to subtotal gastrectomy with relief. Two jejunal ulcers followed pylorectomy with Billroth-II anastomosis—one after 18 months and the other after two years, both should be reoperated upon.

Only one jejunal ulcer has so far developed following partial resection and that came three years after the first operation. This man had about a quarter of his stomach removed. It is our belief that he has antial hormone cells remaining in his proximal segment, and this is some argument in favor of removing at least the distal half of the stomach.

The other poor result followed a partial resection of the Polya type. The patient was entirely relieved for four years, but since then has had several massive hemorrhages. He has recently entered another hospital for further treatment.

TABLE VI

DUODENAL ULCERS

Massachusetts General Hospital

RESULTS (1938-1941)

Subtotal resections	76
Deaths	5
Present Status	
Poor in one case (postoperative common duct stricture)	
Excellent in all others	
Six to 12 months are required to regain appetite and weight	

During the 34 months not included in the follow-up table, we have had 76 subtotal gastrectomies for duodenal ulcer with five deaths. None of the survivors has been invalided since, save the man whose common duct was sectioned and reanastomosed to the duodenum. He had signs of cholangitis, and may continue to have disability from this complication although a cholecystojejunostomy has been performed recently. It is interesting to note that some patients are able to return to work in three months, although it takes from six to 12 months for these individuals to get so they can get along

on three full meals a day and gain weight. There is also a lag-period as regards appetite. This, we believe, is due to the interference with the nerve supply to the remaining proximal segment. It is amazing, however, to see these people eat a large meal and enjoy it without distress after they have become adjusted to their new arrangement. So frequently these individuals want to know why surgery has been withheld from them so long. Little do they realize what a stormy convalescence some of the survivors have had.

SUMMARY AND CONCLUSIONS

(1) Cases of duodenal ulcer now requiring surgical treatment represent about 20 per cent of all patients with this lesion coming to a large urban hospital.

(2) Acute perforation accounts for about one-fourth of these operative cases.

(3) Cicatricial obstruction from duodenal ulcer, usually of long standing, is the indication for operation in one-third of the remaining cases.

(4) Intractability and massive hemorrhage make surgery necessary in the remaining cases and these represent less than 10 per cent of all duodenal ulcer patients.

(5) In this last group, palliative operations such as gastro-enterostomy, pyloroplasty, gastroduodenostomy, local excision (even with the pylorus), transection for exclusion, and gastric resection for exclusion, without removal of the antral mucosa, are all attended with a high percentage of persistent symptoms and anastomotic jejunal ulcer.

(6) The mortality following subtotal gastrectomy for duodenal ulcer in the Massachusetts General Hospital was not greater than that following less extensive operations.

(7) In those cases operated upon from three to nine years prior to this report, the results of true partial gastrectomy were excellent or good in all but two cases.

(8) Two-thirds of 67 jejunal ulcers following palliative procedures for duodenal ulcer occurred within two years of the original operation in our clinic.

(9) In 71 survivors of 76 subtotal resections performed during the past 34 months, no jejunal ulcer has thus far developed. This, we believe, is the procedure of choice. Certainly, not less than half the stomach together with the pylorus should be removed when feasible.

(10) In complicated, extensive ulceration, one is justified in resection for exclusion provided the antral mucosa is removed at the original procedure, or that the whole remaining distal segment is removed as a second stage six to eight weeks later.

(11) Our poorest results were in those cases with resection for exclusion without removal of the antral mucosa—five jejunal ulcers in nine operative survivors.

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DISCUSSION—DR FREDERIC W BANCROFT (New York, N Y) I should like to report a case that is rather historic This patient had a lesser curvature ulcer and was operated upon by me in 1930 A high subtotal gastrectomy was performed Dr Lewis Gregory Cole took sections from this ulcer, half from one side and half from the other, and sent the sections to a number of pathologists without giving any identification or history On one side, all pathologists were agreed that it was benign, whereas on the other side, 75 per cent diagnosed some type of carcinoma This patient presented himself to my office recently, after having had three severe gastric hemorrhages Roentgenograms do not show definitely any ulcer, and gastroscopy was negative In going into this patient's history I have learned that he has been on a very low vitamin diet, and it is possible that his hemorrhages at the present time are not due to a jejunal ulcer or to recurrence of the carcinoma

I should like to say a word about the modified Devine operation Recently, in order to remove more of the pyloric antrum, I have mapped out an area in the prepyloric zone which would be sufficient, after denuding the mucous membrane, to allow a triple inversion The stomach is transected at this portion, then further stomach is removed toward the cardia in order to give sufficient excision of the stomach I think this procedure has certain advantages There is usually no difficulty in a duodenal ulcer in removing this portion of the stomach I had one patient that suffered from a hemorrhage where I had left too large a cuff at the prepyloric region Also, one

must warn against too far exploration if this procedure is decided upon, because in the only sure death I have had I explored the duodenum rather thoroughly before attempting the operation. The patient died five days later of peritonitis, and at autopsy it was found that he had perforation of the duodenal ulcer. I think I caused this perforation by too much exploration.

DR R. L. SANDERS (Memphis, Tenn.) Doctor Allen and Doctor Walters have given us two interesting and worthwhile papers. My remarks will be devoted to Dr. Allen's paper, emphasizing two points. First, a definite swing from gastro-enterostomy to partial resection in the treatment of duodenal ulcer, and second, the necessity for removal of the pylorus and the ulcer.

Recently we reviewed a series of 110 surgical cases of duodenal ulcer covering the years 1925 to 1934, inclusive. It was found that gastro-enterostomy was performed in 102 of these, and resection in only eight. In a similar study of cases covering the period of 1935 to 1940, there were 29 resections as compared to 31 gastro-enterostomies, or practically an equal use of both procedures in the treatment of duodenal ulcer. Our results have justified this change in the type of operation.

Regarding the necessity for removal of the pylorus, in a follow-up of the above mentioned 29 patients who had had resections, two were found to have a poor result, in neither case had the pylorus been resected.

One of the cases of the earlier group was so unusual and so well illustrates this point that I shall report it briefly. The patient had had a gastro-enterostomy in 1918 for a nonobstructing duodenal ulcer associated with high acids. He developed a gastrojejunal ulcer and came to us for treatment. We performed a partial gastrectomy but did not remove the pylorus because of technical difficulties. Later, another gastrojejunal ulcer developed and perforated, and a second resection was carried out, the ulcer being removed with a little more of the stomach and the anastomosis reset. Still later, the cycle was repeated and resection was performed the third time. Again, an ulcer formed and perforated. By this time, which was in 1931, the patient was tired of being operated upon for ulcers, for which I could not blame him. He went elsewhere and had both adrenals denervated. His pain continued, however, and he became a morphine addict. He died two years ago, still unrelieved of his suffering. Had we removed the pylorus at the first resection the whole course probably would have been different. It is now our practice and teaching to remove, when possible, the pylorus as well as the ulcer in all stomach resections.

DR ROBERT L. PAYNE (Norfolk, Va.) I wish to ask a question which I think is of interest to every man here who does not do as many gastric resections as the essayists. The problem which concerns me is the satisfactory closure of the duodenal stump. Doctor Walters stated that the risks involved in resection for carcinoma were less than in resection for ulcer of the duodenum because of the ease of closing satisfactorily the duodenal end of the resection. I am impressed with the fact that the danger of leakage, with peritonitis, or the development of a duodenal fistula centers around the proper and satisfactory closure of the duodenal stump. Doctor Allen reported one case of duodenal fistula with death, and stated that he had devised a means to circumvent this in the future. I would like him to explain that statement—whether he divides the duodenum above the ulcer in healthy structures, does a Finsterlein exclusion, or exactly what method he has devised to overcome the danger of leakage from the duodenal stump.

DR ARTHUR W ALLEN (Boston, Mass., closing) Doctor Bancroft cited the case of a jejunal ulcer coming years after subtotal gastrectomy for gastric "ulcer-cancer." This is so unusual that I wonder if, by any chance, a small segment of antrum remained. We have a patient with anastomotic ulcer following subtotal resection for acute massive bleeding from gastric ulcer and, on reviewing this case, we find that we had left a small remnant of the antrum. Jejunal ulcers are very rare following any operation for gastric ulcer.

Dr Sanders' case report is duplicated in our paper, except that in our case the patient came back and we resected the pylorus and the second jejunal ulcer on the third operation, and he has remained well since. One man had had three resections elsewhere before he came to us. He had a jejunal ulcer that had developed very quickly after the third operation, and I suggested that we do nothing except remove the pyloric segment, which we surmised had been left at his original resection. He was relieved immediately following its removal. The stomal ulcer healed without reoperating upon the stoma, much to our surprise and has remained healed for 15 months.

Doctor Payne's question involves a lot of time for discussion and can be answered only in a general way. One must determine the location, extent of inflammatory reaction, and the neighboring structures involved before deciding the type of operation to undertake. The ideal situation is one that allows resection beyond the ulcer, leaving at least three-quarters-inch of normal duodenum to invert. Two rows of carefully placed catgut sutures, both introduced so that peritoneal surfaces are held in contact, and so that all the mucosal edge is turned in, will ensure healing with no fear of blowing out. The reaction caused by the catgut in these healing serious surfaces may enhance adherence and seal the surfaces more securely. Silk or cotton, with their greater tendency to cut through delicate structures and their lack of reaction, may make them less useful for this purpose than one would expect. I have very rarely found sufficient normal duodenum to work with to use the ingenious instruments devised for inverting the duodenal stump.

Doctor Bancroft has brought out the danger of late perforation if one undertakes too much dissection in the region of the ulcer, and then finds that he must limit the operation to resection for exclusion. We have made the same error in one case with fatal perforation three days after operation. On occasion, one can see by the extent of the inflammatory reaction that an attempt to resect beyond this would, at least, be tedious and possibly dangerous. One can, however, free the lateral border of the duodenum as first described by Doctor Finney in his pyloroplasty operation, and determine the entrance of the common duct into the duodenum. This is harmless and often settles the question regarding the proper procedure in that particular case.

If, in order to be sure of a comfortable closure of the distal segment, one must resort to resection for exclusion, then two choices are available. One may denude the remaining antrum of its mucosa and hope to cure the patient at one operation. Due to the thinness and friability of the remaining peritoneal and muscular coats of this segment, I have sometimes been unhappy about the type of closure that could be obtained. Some of our cases have had their convalescence lengthened on this account. The remaining choice is a deliberately planned second stage, six to eight weeks later, for the removal of the antral segment. McKittrick thinks well of this two-stage operation at the moment, and may be able to demonstrate that this is not only the safest procedure in complicated cases but that the actual time involved may not be too much increased.

DR WALTMAN WALTERS (Rochester, Minn., closing) I just want to clarify a point mentioned by Doctor Payne, namely, that the risk of resection of the stomach, or partial resection for carcinoma, is greater than for benign gastric ulcer or duodenal ulcer. The risk for resection of the stomach in cases of chronic gastric ulcer is less than in cases of duodenal ulcer. The reason for this is the difficulty of closing the duodenal stump and, because of foreshortening of the duodenum by the ulceration, the possibility of leakage of the duodenal contents.

The results of resection of the stomach for gastric ulcer are well-nigh perfect. I have never seen a case of recurring ulcer in which a subtotal gastrectomy has been performed for benign gastric ulcer. On the other hand, although I have an optimistic view of the results of the surgical treatment of duodenal ulcer following partial gastrectomy, yet I want to call attention to the fact that recurring ulceration does take place. In a group of cases of gastric resection studied by Lewis and me, it was found that recurring ulceration took place in 2 per cent of cases. In a very interesting monograph by Stirling, he summarized the results of resection of the stomach and duodenum in 25,000 cases of duodenal ulcer and gastric ulcer operated upon in central European clinics. In that series the recurrences were 2 to 2.5 per cent. In other words, resection of the stomach for duodenal ulcer is not the complete answer to the prevention of recurring ulcer. However, the results so far suggest that one must take into account that the recurrence rate is very small, with a reasonably low mortality rate, and the results are usually excellent.

SARCOMA OF THE SMALL INTESTINE ⁺

REPORT OF FOUR CASES

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THIS PAPER IS based upon a careful study of the cases of primary sarcoma of the small intestine as reported in the past ten years, and an analysis of four cases which we wish to add to the literature. A thorough study of all publications, from 1932 to August, 1941, was made in order to learn how many cases of sarcoma of the small intestine had been recorded. There are 114 cases reported. Two of these, each published in two different journals, both foreign, are counted only once. The details of 102 cases are reported, and 12 others are mentioned, six by Medinger, three by Boyce and McFetridge, two by Sanchez, and one by O'Herne. Sufficient data are not presented in the papers of these authors for us to include them in any detailed study.

Crowther, in 1913, collected 191 cases of sarcoma of the intestine of which 117 were in the small bowel. Graves, in 1919, reviewed the literature and recorded 249 cases including three of his own. Ullman and Abehouse, in 1932, collected an additional 125 cases of intestinal sarcoma and added one. It was interesting to note that in reports by three different authors it was stated, "this is the 276th case." We wish to call attention to the fact that the contributions of Graves and also that of Ullman and Abehouse are concerned not with sarcoma of the small intestine but of the entire intestinal tract. Ullman and Abehouse state that of their collected cases only 77 were in the small intestine, and they added one case of lymphosarcoma of the ileum. It has been impossible for us to review all of the literature previous to 1932 in order to present the exact number of cases of sarcoma of the small intestine on record. We probably have overlooked some cases reported since that date but, if so, it is due to the fact that the title of the paper was misleading.

It has been the observation of many investigators, including Corner and Fairbanks, that the incidence of the ratio of sarcoma of the small to sarcoma of the large intestine is 2:1. If we should start to figure from the report of Graves we would conclude that of his 249 cases only 166 were in the small bowel. Ullman and Abehouse add 77 cases, making a total of 243 cases on record up to 1932. We have investigated all reports since that date and have

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941.

collected 114 cases and are adding four more, making the probable total cases of sarcoma of small intestine on record 361

Sarcoma of the small intestine is rare Perry and Shaw, quoted by Bill, investigated the autopsy records of Guy's Hospital from 1826 to 1893, and found only six cases of sarcoma of the small intestine in 17,652 necropsies Libman states that there were no cases observed in the Berlin Pathological Institute from 1859 to 1875, and Nothnagel reported only nine in 21,358 autopsies in the General Hospital of Vienna from 1882 to 1893 In the Prague Pathological Institute, from 1883 to 1898, Smoler found 13 cases in 13,036 postmortem records In the New England Deaconess and Palmer Memorial Hospitals, from 1927 to 1939, Medinger was able to find ten malignant tumors of the small intestine at autopsy, and in the surgical material studied there were 12 instances In other words, in 42,456 examinations he found 22 cases of malignancy of the small intestine and of these only six were sarcomata Chont in a review of 2,252 necropsies and 20,603 surgical specimens from the University of Oklahoma Hospital found only eight tumors of the small intestine including four sarcomata

Sarcoma of the small intestine occurs more frequently in males Chont places the ratio of males to females as 3 2 In the cases we reviewed there were 75 males and 27 females, a ratio of practically 3 1 This is in accord with the findings of Speese and Graves (Table I)

TABLE I
SARCOMA OF THE SMALL INTESTINE
1932-1941

Cases available for study	102
Males	75
Females	27
Ratio Males to Females	3 1

The disease is more common in the middle-aged Relatively few cases were observed in individuals under age 30 Our findings agree with those of Cameron who states that infants and children comprise 10 per cent of the cases of sarcoma of the small bowel From our studies it is evident that 50 per cent of the cases of small intestinal sarcoma occur between the ages of 30 and 60 The average age of males was 41+ and of females 43+ years (Table II)

TABLE II
SARCOMA OF THE SMALL INTESTINE AGE INCIDENCE

1-10	13
10-20	1
20-30	9
30-40	19
40-50	16
50-60	26
60-70	13
70+	5

Average Age Males 41+ Females 43+

Trauma is thought to be a causative agent of small intestinal sarcoma Boyce and McFetridge mention this as an etiologic factor Ullman and Abehouse are also of the opinion that trauma plays an important rôle in the pro-

duction of the disease and state that it occurs more frequently in the working class. Zwalenburg records a case occurring in a child six weeks after injury. Peterson writes of three patients who developed intestinal sarcomata six to ten weeks after abdominal contusion, and Vercellotti agrees that trauma is a most important factor in the production of sarcoma of these structures. We could obtain no history of abdominal injury in our cases although three of them occurred in individuals of the working class.

Symptoms—The onset of symptoms may be sudden, due to perforation, severe hemorrhage, or acute intestinal obstruction. Usually, however, the disease is insidious in onset and is characterized by griping pains in the abdomen and occasional attacks of nausea and vomiting, loss of weight and strength, and anemia. Frequently there is change of bowel habit, with attacks of diarrhea. If the disease is widely disseminated there may be some elevation of temperature.

The symptomatology varies depending upon the site of the lesion. When the duodenum is involved vomiting and jaundice may be early symptoms, simulating gallbladder disease. When the tumor is located in the lower jejunum or ileum the first symptom may be the appearance of a mass in the abdomen, for instance, Case 3 of our series was referred with a diagnosis of appendiceal abscess. He had abdominal pain, vomiting, some fever, and a mass in the lower right abdomen.

Not infrequently acute intestinal obstruction causes the patient to consult a physician. Obstruction is rarely due to the growth itself although the tumor may be the cause of intussusception. The obstruction frequently is due to kinking and, consequently, the formation of adhesions between adjacent loops of small bowel. Also, when the tumor grows it extends along the submucosa infiltrating it and the other layers of the bowel, and as a result we get the formation of a rigid tube of varying length in which no peristalsis occurs and obstruction supervenes. Other causes of intestinal obstruction due to sarcomata are compression of, or, encroachment on, the lumen, and frequently the presence of small or large annular masses. Cameron states that the annular constricting type of sarcoma of the small intestine is much more frequent than that type characterized by an aneurysmal dilatation of the intestine.

Chemical examination of the stool usually reveals the presence of blood. Occasionally, the first evidence of the disease is a massive hemorrhage, such as occurred in our Case 2, and in the case reported by Mahaffey.

Perforation is rare. Chont was able to collect from the literature only seven cases of intestinal perforation due to sarcoma. Case 1 of our series was operated upon for an acute intestinal perforation. In addition to those enumerated by Chont (Hulbert, Pissarewa, Premoli, Whitaker and Fischer, Oettle, Davis, and Lewis), we also found reports by Leveuf and Godard, and by Goldsmith, in which perforation was followed by a localized abscess. Other perforations are reported by Frankman and Drummond, Monad and Arnal, Mumey, and Basabe.

The diagnosis of small intestinal sarcoma is made on the history of abdomi-

nal pain, blood in the stools, some loss of weight, and the presence of an abdominal tumor. The location of the tumor varies. It may be palpable one day and not the next. This is because the weight of a growth in the jejunum or ileum would naturally predispose to its location within the pelvis and it would be evident only when distention of other intestinal loops force it out of the pelvis. In one of our patients the tumor was palpable on one occasion and at a later examination could not be felt at all.

Most of the cases of small intestinal sarcoma are not diagnosed previous to operation. The earlier writers decried the value of roentgenologic studies in these cases, however, within recent years roentgenologic examination of the small intestine has become valuable. Medinger states that such studies are of value in 50 per cent of cases, and Cameron emphasizes the importance of such studies. It has only been within the past few years that roentgenologists and clinicians have realized that much information can be gained by roentgenologic study of the small bowel. Cohn, Landy and Richter urge that this be done in all cases presenting intestinal symptoms.

Roentgenologic Diagnosis of New Growths of the Small Intestine—The roentgenologic diagnosis of new growths of the small bowel may be divided into two groups: (1) Those causing a high degree of obstruction at the site of involvement, and (2) those in which obstruction is not a factor of importance.

The site of those lesions which cause a high degree of obstruction may be demonstrated at times by so-called preliminary or plain films of the abdomen made with the patient horizontal and upright. In such cases distended loops of the small bowel may be seen and the approximate site of obstruction indicated by their appearance and by the point at which the column of gas ends. The mucosal folds of various parts of the small bowel differ quite markedly in appearance, and this characteristic is of aid in localizing the growth. Obstructive lesions may demand further investigation. Some have been demonstrated by giving a small amount of barium by mouth, then tracing the column downward to the point of obstruction. This method is now seldom used and can be dangerous. The safest procedure is to pass a Miller-Abbott tube into the small intestine and to trace its progress downward, decompressing the bowel en route, until the progress is arrested. The lesion itself then can frequently be outlined by injecting opaque material through the tube.

In nonobstructing new growths the only satisfactory method of demonstration is the so-called "small bowel study." In this method from 90 to 180 cc. of an aqueous suspension of barium sulphate is given by mouth and the progress of this material through the small intestine is observed at frequent intervals, the interval between observations varying with the condition found in each case.

When a new growth in the duodenum is a consideration, serial films of the entire duodenal area are essential, inasmuch as early lesions may manifest themselves only by distortion or obliteration of the mucosal folds in the affected areas. In the jejunum and ileum, in addition to the conventional films, those

made with localized pressure over portions of the bowel that seem to be abnormal may be of great benefit in arriving at a definite diagnosis

Nonobstructing new growths of the small intestine manifest themselves by deformity of the lumen, obliteration of the mucosal folds, or by evidence of mild interference with the progress of the column where an appreciable degree of obstruction is not present

Pathologic Types of Lesions—In 102 cases that we studied the pathologic type of the growth was stated. There were 66 lymphosarcomata, and three reticulum cell sarcomata. These are both of lymphoid origin, hence it may be said that more than 50 per cent of cases of small intestinal sarcomata are of the lymphoid type. Twenty-three cases were thought to originate in the musculature and are listed as 22 leiomyosarcoma and one myosarcoma. Ten cases are listed as follows: Fibrosarcoma six, neurofibrosarcoma three (two of which were reported by the authors) and one spindle cell sarcoma. It is exceedingly difficult to say with any certainty whether a growth is a leiomyosarcoma or a neurofibrosarcoma. The very best pathologists disagree as to the exact classification of these tumors but all agree that they are sarcomata, in other words many reported as leiomyosarcoma may be fibro- or spindle cell sarcoma (Table III)

TABLE III

SARCOMA OF THE SMALL INTESTINE	HISTOLOGIC TYPES
Lympho-	66
Reticulum cell	3
Leiomyo	22
Myo-	1
Fibro-	6
Neurofibro	3
Spindle cell	1
Total	102

Location of the Lesion—In the series under discussion the lesion appeared in the duodenum 21 times, in the jejunum 26, and in the ileum 41 times. In one case the exact location of the lesion was not stated. There were two instances in which Meckel's diverticulum was the site of the primary growth. Sarcoma, in contradistinction to carcinoma, not infrequently appears as multiple lesions and may even occur in all parts of the intestine (Table IV)

TABLE IV

SARCOMA OF THE SMALL INTESTINE	LOCATION
Duodenum	21
Jejunum	26
Ileum	41
Not stated	1
Jejunum and ileum	2
Meckel's diverticulum	2
Duodenum and jejunum	4
Small intestine	4
Duodenum and ileum	1

SARCOMA OF SMALL INTESTINE

Lymphosarcoma of the Small Intestine—Since the ileum contains numerous lymph follicles one would naturally conclude that this part of the small bowel would be a common site for malignant lymphoid tumors. An investigation of the 69 lymphosarcomata recorded during the past ten years reveals the fact that 32 of them occurred in the ileum, and where the lesions were multiple, ten more occurred in the ileum and other parts of the small bowel. The duodenum was the site of lymphosarcoma in 11 instances and the jejunum in 16 (Table V)

TABLE V
 LYMPHOSARCOMA OF THE SMALL INTESTINE LOCATION

Duodenum	11
Jejunum	16
Ileum	32
Multiple areas including ileum	10

In the literature there has been considerable discussion as to the rarity of leiomyosarcoma and its location. In the cases reviewed 23 were myogenous in origin and occurred equally in the three subdivisions of the small bowel. Seven occurred in the duodenum, seven in the jejunum, and seven in the ileum. In one case there were multiple lesions in the jejunum and ileum, and one case originated in Meckel's diverticulum (Table VI)

TABLE VI
 MYO- AND LEIOMYOSARCOMA OF THE SMALL INTESTINE LOCATION

Duodenum	7
Jejunum	7
Ileum	7
Jejunum and ileum	1
Meckel's diverticulum	1

The fibrosarcomata, including the neurofibro- and spindle-cell sarcoma, occurred practically as frequently in one part of the small intestine as in another. Three originated in the duodenum, two in the jejunum, and four in the ileum, and in one case multiple lesions occurred in the jejunum and ileum (Table VII)

From these statistics one must conclude that, other than lymphosarcoma, all other types occur as frequently in one part of the small intestine as another. The high incidence of lymphosarcoma in the ileum is easy of explanation.

TABLE VII
 FIBROSARCOMA INCLUDING NEUROFIBRO- AND SPINDLE CELL OF THE SMALL INTESTINE LOCATION

Duodenum	3
Jejunum	2
Ileum	4
Jejunum and ileum	1

Pathology—The sarcomata which are possible in the small bowel according to histogenesis are Lympho-, neurofibro-, leiomyo-, reticulum, fibro-, endothelial, lipo-, and neurosarcomata. The last two named, one derived from

fat tissue, the other from nerve ganglia in the bowel wall, seem not to have occurred, or to have been reported, so there is no basis for description.

Lymphosarcoma—The bowel may be involved in a very widespread sarcomatosis of the lymphoid type, but in this condition the primary focus is usually elsewhere and the bowel lesions are commonly symptomless. Lymphosarcoma may occur primarily in the lymphoid tissue of the small bowel, and, if so, it is inclined to remain localized to this part of the bowel only, or to the bowel and adjacent nodes, in contrast to the very widespread lesions that characterize this tumor when originating elsewhere.

The mass is soft and friable, resembling lymphoid tissue, but of a lighter gray color. Friability is lost if there is much stroma or if the tumor infiltrates the muscle. The bulk of the tumor tissue is in the mucosa and submucosa, sometimes encroaching on the lumen by a complete tube-like layer inside the muscularis, but infiltrating it. Usually tumor is noted in the serosa either in small nodules or a large mass. Obstruction is common and is produced by destruction of the bowel wall and kinking, or by tumor mass protruding into the lumen. Ulceration is frequent and perforation by necrosis of tumor may occur. The growth is not sharply limited as a rule because of infiltration or, perhaps, because of gradual neoplastic development in the lymphoid tissue at the periphery of the primary focus.

The parenchymal cell is the lymphocyte and usually differentiation is sufficient to make diagnosis definite. The cells may be only slightly larger than normal or markedly larger, in which case the term "large cell" sarcoma has been used. Nuclei are round, moderately hyperchromatic, and mitotic figures are common. Cytoplasm is not abundant, but if the cells are large it is moderate in amount and stains faintly. At the periphery of the tumor the stroma consists only of invaded tissue. If this has been destroyed the stroma consists of a large amount of new connective tissue and in areas is not visible at all in ordinary stains. Vascular supply is very meager and the few vessels consist of an endothelial lining without much support. Hemorrhage is, therefore, common, but not massive.

Since the growth is somewhat less malignant than lymphosarcoma elsewhere and tends to remain localized in the bowel, obstruction occurs and resection is warranted and may be successful.

The accepted cell origin of this neoplasm is the lymphocyte of the lymph follicle, however, it has been stated that origin may be independent of them. The explanation is that lymphosarcoma may develop from infiltrating lymphocytes in tissues other than lymph follicles. This has been observed in the prostate where there is no lymphoid tissue normally.

Reticulum Cell Sarcoma—This tumor may be classified as a type of lymphosarcoma, although others designate it as a type of fibrous connective tissue growth. Whatever its true nature may be, the diagnosis is one that can be made only with the microscope. Its peculiarity consists of a varying amount of delicate reticulum which is made visible by silver staining. The parenchymal cells resemble lymphocytes but the stroma is more abundant than

in the lymphosarcoma, however, it is not dense. The gross appearance is identical to that of lymphosarcoma except that it may be less bulky, slightly more firm, and more localized.

Leiomyosarcoma—Smooth muscle tumors may be single, but are prone to multiplicity. The malignant ones are very seldom pedunculated, but do have considerable mass which may protrude into the lumen of the bowel or bulge on the exterior. Some descriptions indicate that there is little mass, but much destruction and replacement. The consistency is distinctly softer than that of benign tumors of the same type, though it is often described as firm. Obstruction is produced by extension into the lumen since there is usually displacement because the rapidity of growth exceeds the destruction of normal tissue and necrosis of the tumor. Obstruction by angulation and kinking is recorded, but is less characteristic of muscle tumors. Ulceration and moderate hemorrhage are common.

The cells are arranged in bundles extending in different directions, and supported by a small amount of connective stroma, in which vessels are in moderate numbers. Nuclei are elongated and rounded with a stippled chromatin pattern. Mitoses are much in evidence and multinucleated giant cells result from incomplete division. The cytoplasm is an elongated fibrillar structure resembling muscle cells, or may be polyhedral, but not stellate shaped. Malignancy is not high grade as a rule so that resection is successful. The very malignant sarcoma of this type is rare.

Fibrosarcoma—This tumor has a wide variation in malignancy, but purely benign tumors of this type are quite rare. Their behavior, then, is quite variable. The less malignant specimens are encapsulated, light colored, and hard. They displace tissue, infiltrate slightly, and grow slowly. The location is exterior to the muscle, and they are attached by a broad base.

The type cell is elongated, having several processes. Nuclei are oval, stippled, and mitoses few. Intercellular fibrillar substance taking the specific stain for collagen is a constant feature. Often this substance is abundant and dense.

The more malignant specimens are soft, light-colored tumors, often hemorrhagic and always infiltrating. They occur chiefly exterior or interior to the muscularis, seldom from the fascia of the muscle. The cells are not arranged in any definite fashion, although occasionally bundles are noted. Nuclei are round or oval with dense chromatin material. Mitotic figures are numerous. Cytoplasm is elongated into short processes and there is fibrillar structure which is coarse and stains like collagen. Blood vessels are few, very imperfectly formed so that hemorrhage into the tumor is marked, but massive hemorrhages into the bowel are not likely unless the tumor is traumatized. Necrosis of the central portion occurs, often leaving a peripheral zone of living tumor tissue. Malignancy is high grade and metastases are early.

Neurofibrosarcoma—This tumor has been mentioned in the literature for over four generations and intestinal lesions of this type were pointed out by von Recklinghausen. Most commonly there are multiple tumors in the body,

but they may be multiple in the small intestine only, or solitary in this organ. The gross characteristics are variable. Certain examples are encapsulated, gray-colored, friable tissue that is very vascular and contains large lakes of blood and blood extravasations. The common origin is from the nerve trunks in the muscle coat. They may protrude as pedunculated tumors into the peritoneal cavity and interfere little or none with the passage of bowel content. Those of higher grade malignancy invade and destroy the bowel wall, then protrude into the lumen, causing obstruction, or form a band-like section several centimeters in length. The mass may be as large as 25 cm in diameter and become adherent to neighboring structures. Necrosis with hemorrhage in the center is frequent, often leaving only a shell of living tissue at the periphery. If the bowel wall is invaded this necrotic tissue may be discharged into the lumen and thus ulceration is started.

The parenchymal cell is large, often stellate-shaped, having blunt processes. Nuclei are elongated and have stippled chromatin patterns. Mitoses are occasional. The stroma is a small amount of new connective tissue in which there are many large blood vessels and cavernous spaces often lined only by endothelium. The cells are arranged into imperfect whorls and interlacing bundles. Palisading is the rule, but is variable in prominence. Metastases may be none, or if few confined to the regional lymph nodes. Rarely are they extensive if the primary tumor is in the small bowel.

In other instances the mass is small, hard and gray-colored, grossly resembling a scirrhus carcinoma. There is obstruction produced by destruction of the bowel on one side, infiltration, contraction and kinking. The growth is slow so that dilatation and hypertrophy result above the lesion.

Microscopically, the structure is similar. There is the usual palisading, the oval, stippled nuclei, but cells are elongated chiefly. Vessels are few, but thin-walled, and hemorrhage is less. Ulceration and perforation are not usual, but may occur in the more malignant tumors.

If tumors are multiple, and they may be very numerous, and if secondary masses are retroperitoneal, growth is rapid and the usual cachexia ensues unless obstruction intervenes. Obstruction may be delayed for a time by necrotic tissue sloughing into the lumen, leaving short sections of bowel wall composed of neoplastic tissue only. More often than not the tumors are single or few, and malignancy is not of high grade, making resection possible.

Endothelial Sarcoma—There are no criteria by which the lymphangio-endothelioma may be distinguished from the hemangio-endothelioma except by the content of the vascular structures which may be formed by the tumor cells. The term angiosarcoma avoids this tissue and may be used to designate vessel formation in contrast to the diffuse type of structure consisting of endothelial cells, but not forming vessels.

It is obvious from certain illustrations in the literature that occasionally epithelial tumors, or carcinomata, are designated as endothelial sarcomata. This error is attributed to the fact that the two types of cells have similar function, namely, that of covering surfaces. Tumors derived from the surface cells

of the peritoneum, or serosa, have been described, but they are widespread growths not limited to the bowel alone and so do not come within the scope of this discussion

If malignancy is low grade the tumor may be discolored by hemorrhage, or have blue areas from blood in large spaces. Usually the tumor is firm and light colored because of the lack of blood. The appearance is granular or nodular and distinctly infiltrating. In the diffuse type there is no nodulation and the consistency is soft. Obstruction may occur from thickening of the bowel wall by infiltrative growth.

In the diffuse type the cells are polyhedral, have clear cytoplasm, and are not organized into any tissue structure. It is evident that this tumor has been designated as a large, round cell sarcoma or lymphosarcoma. The vascular forms are composed of flat cells also with clear cytoplasm, usually having hyperchromatic nuclei, and they are arranged into whorl, or pearl-like masses, by layering about a focus or lumen of a vessel. Excision is difficult because, grossly, the boundary is not readily visible. Delicate processes extend along fascial planes for some distance, and are amputated when the main mass is removed, thus making recurrence frequent. Metastasis of the vascular types is not common or widespread. The diffuse growth is quite malignant.

Hodgkin's Disease—Since the small bowel contains lymphoid tissue, it is conceivable that Hodgkin's disease could begin here. The literature contains several reports which will admit of this interpretation, but the regional lymph nodes were involved also, therefore, it is not possible to state with certainty that the disease did not begin in the lymph nodes and produce secondary foci in the bowel. Also, there is the problem of stating what is the nature of Hodgkin's disease. Evidence of its being a true neoplasm or a chronic infectious granuloma is ponderous and inconclusive. Recently the argument has been avoided by accepting the view expressed by Ewing that Hodgkin's disease of the lymph nodes is primarily an infectious granuloma of unknown etiology, that it may remain as such, or it may become neoplastic and then properly be called Hodgkin's sarcoma, which he considers to be of endothelial origin and could be classed with the endotheliomata. The cells, however, have lost their endothelial characters.

The growth involves the lymphoid tissue of the bowel chiefly, but is invasive into surrounding structures. It produces obstruction by mass protrusion into the lumen and thickening of the bowel wall by tumor growth. The histologic structure is identical with the same lesion in the lymph nodes. Fibrosis is present, but to a variable degree, or if marked, there is a dearth of parenchymal cells. These consist of a few large and small lymphocytes, an occasional plasma cell, proliferating endothelial cells, and occasional multinucleated giant cells having vesicular or hyperchromatic nuclei. These cells have been termed Steinberg giant cells and Dorothy Reed giant cells. Rather abundant are large mononuclear cells of the same type. These cells are characteristic, but their exact nature is not agreed upon. They have been regarded as derivatives of endothelial cells, reticulum cells and lymphocytes. As the disease

progresses lymphocytes tend to disappear and the characteristic cells to become relatively more numerous. Polynuclear neutrophils and eosinophils may be present, but are not essential.

COMMENT—Neurofibrosarcoma is generally accepted to be of nerve sheath origin (sheath of Schwann) and recently has received much attention. Reports of its appearance in various parts of the body are almost daily occurrences and the list is growing larger chiefly at the expense of the lists of fibrosarcomata and leiomyosarcomata. The fibromata of the ovary and the kidney are the only ones that have not succumbed to the modern fashion of the alias.

Reports and illustrations in the literature are not sufficient in detail to permit of analytical study and reclassification, yet if this were possible the present-day lack of uniformity of opinion about histogenesis and classification would make the labor fruitless. Hence, any analytical review of the literature at present must be considered to have an erroneous classification of the different types of sarcoma and will continue in error until such time when additional knowledge is at hand to aid in more correct interpretation of cell structure.

At present, the confusion rests chiefly in the differentiation between fibrosarcoma, leiomyosarcoma, and neurofibrosarcoma. Theoretically, histogenesis is clear, but differentiation in neoplastic growth is not definite enough to permit accurate interpretation.

Treatment—There is but one treatment for intestinal malignancy, be it carcinoma or sarcoma, regardless of its location in the small or large bowel—that is radical extirpation. This procedure should include as much of the node-bearing area of the mesentery as possible. From all reports sarcomata of the small intestine other than lymphosarcoma do not metastasize to the nodes early, thus, early excision can be curative. Lymphosarcoma, however, quickly invades the nodes of the mesentery, and also spreads to the liver, spleen, and kidneys, but rarely are the superficial nodes involved. In advanced cases the serosa of the bowel becomes infiltrated by tumor tissue and other structures are invaded by contiguity. Frequently the bladder or other pelvic structures become involved. Stable reports a case in a female, age 76, in which part of the jejunum and a large part of the transverse colon was excised and the patient was well a year later. He states "Operative risk ceases to exist in the face of a lethal condition."

Radiation Therapy—We believe that radiation has a place in the treatment of sarcomata of the small intestine, especially of the lymphoid type. In one of our cases there was wide-spread involvement of the mesenteric lymph nodes, all of which could not be excised. This patient had a moderate dose of postoperative irradiation but died eight weeks later. Two others received radiation and are apparently well.

There are several cases in the literature where the location of the growth prevented its removal and the only treatment was roentgenotherapy. Fair success was obtained. C. W. Mayo mentions a case in which the stomach was involved and treatment with radium was of some value. Minot and Isaacs state that roentgenotherapy alleviates symptoms, diminishes the size of the

growth, and improves the general condition, but does not influence the duration of the disease. Desjardins and Ford believe that, although roentgenotherapy may or may not prolong life, it does keep the disease under control.

Chont discusses radiation therapy of leiomyosarcoma of the small intestine. Geschickter states that they are radioresistant, and Phillips is of the opinion that they are more radioresistant than lymphosarcomata. We believe that no tumor can be classified as radioresistant until treatment is given and the effect noted. As stated previously, it is exceedingly difficult for the pathologist to say whether a tumor is a neurofibrosarcoma, a fibrosarcoma or a leiomyosarcoma. Certain neurofibrosarcomata arising in the superficial nerves are radiosensitive, and one would naturally conclude that such tumors originating in the bowel would likewise be radiosensitive. Hence we are firmly convinced that roentgenotherapy has a definite place in the treatment of intestinal sarcomata.

CASE REPORTS

Case 1—L. S., male, age 45, was seen February 10, 1941, in consultation with Dr. Isadore Goldstein. He gave the following history: He was awakened during the previous night by griping pain in the abdomen. The pain continued at intervals during the night and the next morning he consulted his family physician (not Dr. Goldstein), who gave him a large dose of castor oil. The pain became steadily worse and at noon he quit work and went home. The pain became more intense and at times it was so severe that it would double him up. About 2 P. M. he had a most agonizing pain which bent him double and he could not straighten out in bed.

Further questioning revealed the fact that he had never been subject to indigestion, could eat anything he wanted, never had pain after meals, nor was he troubled with nausea. He did take a laxative about every two weeks, although this was not necessary. There had never been any blood in the stool. The day before the onset of his trouble he did not feel very well, was a little nauseated, but other than that had no complaint. Further questioning elicited the fact that about ten weeks previously he had had a cold and while coughing he noticed a lump appear in the right side of his lower abdomen. This lump he could feel very distinctly. He consulted his physician who strapped his abdomen with adhesive tape, having made a diagnosis of strained muscles. The previous and family histories were essentially negative.

Physical Examination—This revealed a healthy-looking middle-aged man, apparently in extreme pain. He lay with his thighs flexed on his abdomen and stated that he could not straighten out. There was marked rigidity of all abdominal muscles and diffuse tenderness. Rectal examination revealed some induration high up above the prostate. No definite mass could be palpated. A diagnosis of acute abdominal perforation was made and surgery advised.

On admission to the hospital his temperature was 100.2° F., pulse 96, respiration 20. Examination of the heart and lungs revealed no abnormality. **Laboratory Data**: Hemoglobin 90, R. B. C. 4,480,000, W. B. C. 12,200, neutrophils 74, monocytes 8, lymphocytes 18. Urinalysis negative. Blood Kahn negative. **Clinical Diagnosis**—Intestinal perforation.

Operation—Under novocain and nupercaine spinal anesthesia, a four-inch incision was made at the outer border of the lower right rectus muscle. The abdomen contained a large amount of thin, opalescent fluid in which were small drops of oil, which was removed by aspiration. There was a mass about the size of an orange in the pelvis, and some of the epiploic appendages of the sigmoid were adherent to it. The tumor was in the distal part of the ileum. The adhesions between the tumor and the epiploic appendages and adhesions between the tumor and peritoneum covering the bladder were separated, and the tumor itself was delivered from the abdomen. Further exploration

of the pelvis revealed scattered pieces of tumor tissues in the cul-de-sac. All of these were removed. An examination of the intestine revealed no other pathology. The mesenteric lymph nodes were not enlarged. A resection of the terminal ileum was done and a side-to-side isoperistaltic anastomosis was made, using catgut throughout.

The remainder of the fluid in the abdomen was then removed by aspiration. Eight grams of powdered sulfanilamide was introduced into the abdominal cavity and the wound closed in layers without drainage.

Pathologic Examination—Gross. Dr. Laman A. Gray. There was a portion from the small intestine measuring 12 cm long. One end of the intestine, for a distance of 9 cm, was essentially normal except for the gradual appearance of a whitish, thickened condition of the muscular wall until it finally entered a nodule in the bowel wall measuring 6 cm. This nodular tumor had a grayish-white appearance and one side was ragged, having been torn, and containing numerous hemorrhagic spots (Fig. 1). A portion of the intestine for 2.5 cm was present on the other side and showed it to be essentially normal. There were also several small pieces of grayish-white tumor tissue measuring up to 2 cm.

Microscopically, sections from several masses of tissues showed them to have a quite solid appearance, made up of elongated spindle-like cells with rather large vesicular nuclei which were also long and oval. In some areas there was variation in the size and shape of the nuclei, some being quite dark. There were very definite scattered mitoses (Fig. 2). *Pathologic Diagnosis*. Spindle cell sarcoma (this might be considered a neurofibrosarcoma but I am more inclined to the diagnosis as stated).

After a very stormy convalescence, during which he received two blood transfusions, the patient gradually recovered. The wound became infected and drained for some time. He was dismissed from the hospital March 5, 1941, 23 days after admission. Four weeks later roentgenotherapy was begun, and the patient received in all 4,500 r units, delivered through three fields—right anterior, left anterior and perineal. Distance 50 cm, filtration 1 Mm. of aluminum and 0.5 Mm. of copper.

At the present time he is perfectly well. Careful examination of the abdomen fails to reveal the presence of any tumor nor is there any free fluid within the abdomen. The liver is not palpable. Rectal examination fails to reveal any induration in the cul-de-sac. The superficial lymph nodes are not enlarged.

Case 2—H. K., white, male, age 40, was first seen in consultation with Dr. David Cohen of Louisville, February 28, 1941, on account of griping pain in the abdomen. The patient had always been well until about six months ago when he began to have pain and cramps in the right lower part of his abdomen. At this time he was under the care of another physician. Roentgenologic studies of the gastro-intestinal tract revealed some irregularity in the duodenal cap but nothing positively conclusive of ulcer. He was started on an ulcer regimen but did not improve. About three months ago he had a severe hemorrhage from the gastro-intestinal tract. There was no hematemesis, all of the blood being passed per rectum. He was extremely pallid and weak and was given supportive treatment and kept quiet in bed for about three weeks. During this time he continued to have griping pain in the lower abdomen coming on one-half to one hour after meals. His strength gradually improved and he was finally able to be up and about. Ten days ago he was examined by a different roentgenologist. The stomach and duodenum were negative for ulcer. The colon was normal. A study of the small intestinal tract revealed in a large number of films an identical pattern in a loop of bowel which lay in the right lower quadrant. The roentgenologist thought he could palpate a mass. It was at this time that the patient was referred to me.

The patient had lost his appetite because he feared the pain in his abdomen that came on after meals. He was slightly constipated but no more so than he had always been. There were no other symptoms except weakness and loss of 20 pounds in weight. His past, and family histories were essentially negative, other than that his father had died from cancer of the lung at age 62.

SARCOMA OF SMALL INTESTINE

Physical Examination—This revealed a middle-aged man, rather poorly nourished. Examinations of the head, neck, heart and lungs were entirely negative. Examination of the abdomen revealed a mass in the right lower quadrant which was movable and apparently nodular. It was not tender. There were no other masses, no tenderness.

—FIG 1

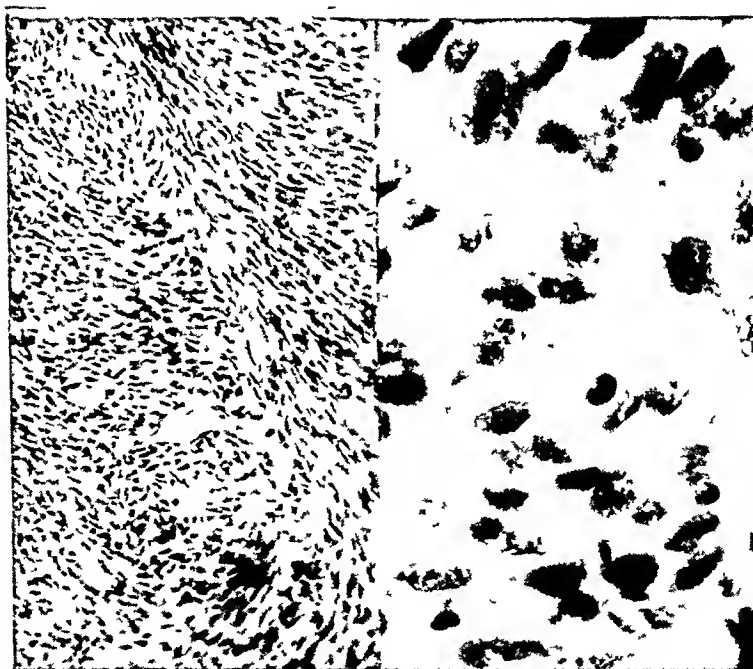


FIG 2

FIG 1—Case 1. Spindle cell (?) (neurofibro or leiomyo) sarcoma of ileum. Normal intestine to the right. Growth of into lumen well shown, also area of hemorrhage.

FIG 2—Case 1. Neurofibrosarcoma of the ileum. Cells are arranged into bundles and whorls. Vessels are numerous. Nuclei are elongated. Chromatin stippled. Much resemblance to smooth muscle cells.

and no rigidity. The liver was not palpable nor was the spleen. There were no enlarged nodes in the groin, axillae or in the neck. *Laboratory Data*: Hemoglobin 62, RBC 4,580,000, WBC 18,450, neutrophils 83, lymphocytes 17. There is some anisocytosis and hypochromia of the red cells. Urinalysis negative. Blood Kahn negative. Blood urea nitrogen 15 mg per 100 cc blood. *Clinical Diagnosis*: Tumor of the small intestine, probably sarcoma.

Operation.—A five-inch incision through the lower right rectus muscle exposed a

tumor of the small intestine about 10x5x5 cm. There were some fine adhesions between the tumor and the epiploic appendages of the sigmoid. The appendages were doubly ligated and divided. The tumor originated either in the lower part of the jejunum or the beginning of the ileum. Grossly, it was yellow in color and was almost completely obstructing the intestine. There were some small soft nodes in the mesentery of this loop of bowel. A wide resection of the small intestine was done including as much of the mesentery as possible. A side-to-side isoperistaltic anastomosis was performed and

FIG 3

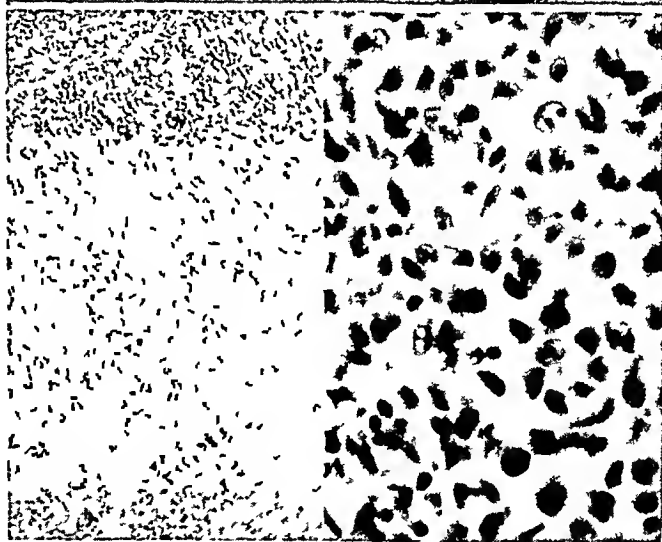
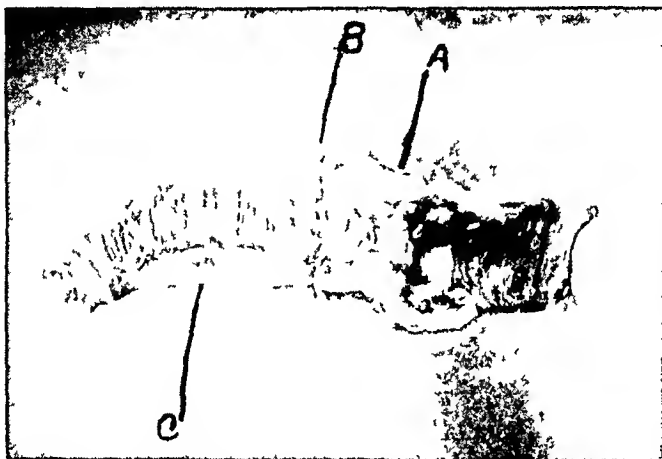


FIG 4

FIG 3—Case 2. Reticulum cell sarcoma jejunum. Dilated jejunum to right. (A) Shows wall infiltrated with tumor. (B) Angulation causing partial obstruction. (C) Secondary small growth of similar type. Hypertrophy of solitary lymph follicles well demonstrated.

FIG 4—Case 2. Lymphosarcoma of jejunum. Cells are closely packed in irregular masses, supported by small amount of new stroma. Cells are round, have delicate cytoplasm. Numerous mitoses.

the opening in the mesentery closed. The liver and spleen were normal. Eight Gm powdered sulfanilamide was put in the abdomen and the wall was closed in layers.

Other than a mild postoperative pneumonia the patient made an excellent recovery and left the hospital 16 days after operation.

Pathologic Examination—Gross. Dr. Harry M. Weeter. Section of small intestine

showed the characteristics of jejunum, consisting of three parts—the proximal portion, approximately 100 Mm in length and open about 75 Mm in width—the distal portion, approximately 200 Mm in length and about 55 Mm in width—and a central tumor mass completely encircling the intestine which, after being incised, measured 100 Mm in length by 95 Mm in width by 20 Mm in thickness. The proximal and distal portions of the intestine had angulated and become adherent to the tumor mass, so that the two portions just touched each other in the side lateral to the mesentery. The inner surface of the mass was slightly necrotic (Fig 3). The cut surface presented a smooth tumor whose point of origin was, grossly, the mucosa. Lymph nodes dissected from the regional mesentery were not enlarged.

Microscopically, the tumor appeared to rise in the mucosa, replacing the latter and infiltrating the submucosa and muscularis, and terminating beneath the peritoneum, the subperitoneal tissue being infiltrated by neoplastic cells. Many of the cells were evidently lymphocytes, others were large, rounded to oval cells with a moderate amount of cytoplasm. There was a fine connective tissue stroma. The cells, in places, seemed to be in contact with the delicate network of the mucosa. In some places they lay loosely in free masses. There was no pronounced alveolar arrangement although some areas suggested this formation. Some nuclei were deeply staining. A number of monasters occurred (Fig 4). *Pathologic Diagnosis* Reticulum cell sarcoma of jejunum.

This patient was likewise given postoperative irradiation of 1,500 r units through each of three fields—right anterior, left anterior and perineal. The factors were the same as in Case 1. Examination nine months after operation revealed no masses in the abdomen or could any tumor be felt in the pelvis by rectal examination. There was no enlargement of the superficial lymph nodes. The patient has gained 18 pounds in weight.

Case 3—R L, white, male, age 18, was admitted to the hospital, August 23, 1941, being referred by Doctor Sweeney, of Liberty, Ky, with a history that two years ago he began to have cramps in the abdomen and vomiting. This was accompanied by chills and fever. He was sick for only a few days and then went back to work and seemed perfectly well until July, 1940. At this time he again developed cramp-like pains in the abdomen and vomited almost continuously for three weeks. He became exceedingly weak and lost 15 to 18 pounds in weight. This attack was diagnosed as gastro-intestinal trouble and seemed to be relieved by treatment. During the past winter (1940-1941) he complained of weakness and fatigue. He gained a little weight but did not feel well. Immediately after eating he would have pain in the abdomen. These symptoms had been practically constant until six weeks previous to admission to hospital when he again began to lose weight and strength.

Three weeks ago the pain in the abdomen became more severe and he began to vomit. Three days previous to admission he noticed a mass in his abdomen just to the right of the umbilicus. This mass was movable, at times being located in the right lower abdomen and at other times being under the right rib margin.

Physical Examination—This revealed a somewhat pale, fairly well-developed, undernourished young man. The abdomen was flat, and in the right lower quadrant was a mass approximately 12 cm in diameter. This was nodular, not tender, and was movable. There was no free fluid in the abdomen. The liver and spleen were not palpable. There was no tenderness or rigidity. The abdomen was reexamined three hours later and at this time the mass was located in the upper right abdomen and seemed to extend beneath the ribs. Rectal examination was negative. *Laboratory Data* R B C 3,350,000, W B C 12,100, neutrophils 62, eosinophils 3, monocytes 3, lymphocytes 30, metamyelocytes 2. Hemoglobin 9.4 Gm (62.6%), color index .94, hemoglobin per red cell .28, platelets abundant. Urinalysis negative. Blood Kahn-negative.

Roentgenologic Examination—A plain film of the abdomen showed a large amount of gas and fecal material in the colon. The bony structures seemed to be normal. Nothing else of importance was noted. A barium enema filled all parts of the colon.

readily. The sigmoid was long and tortuous. The bowel, in general, was hypotonic. The cecum was regular in outline and normal in tone.

Films were made both before and after evacuation. They showed nothing definitely abnormal in the large bowel aside from the fact that a great deal of gas and fecal material were present, evidently indicating that elimination was not satisfactory. The bowel was somewhat hypotonic. Nothing else of importance was noted. No defects were found in the cecum suggesting pressure defects due to extrinsic masses of any type.

An intravenous urinary tract examination was done. The right pelvis was found to be considerably dilated. There was a filling defect that could be due either to intrinsic

FIG 5

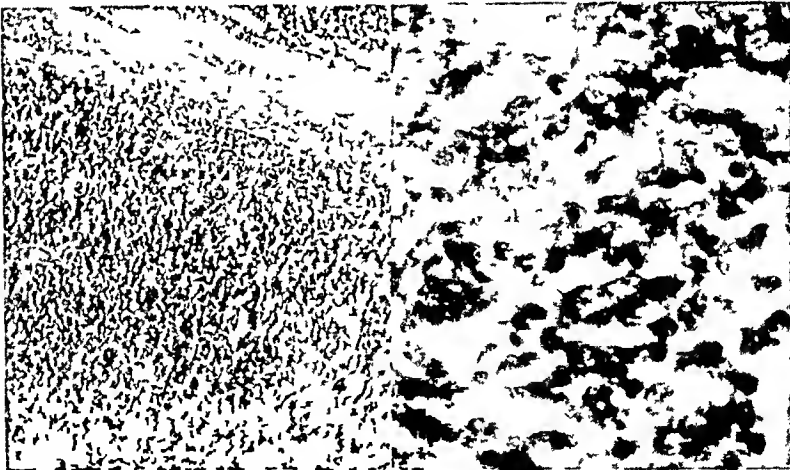
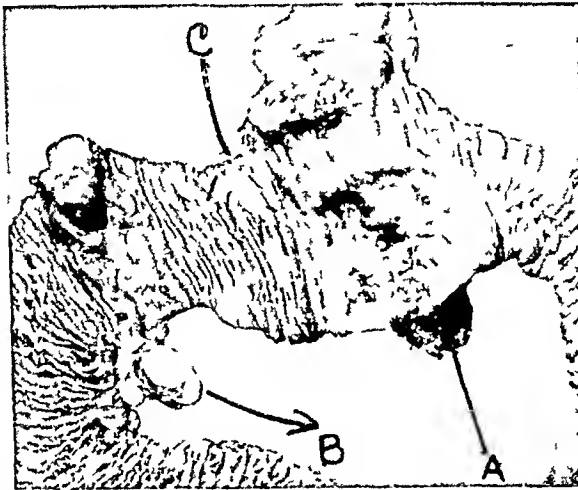


FIG 6

FIG 5—Case 3. Lymphosarcoma of jejunum. (A) Primary tumor causing partial obstruction. (B) Secondary tumors—not uncommon in this type of growth. (C) Hypertrophy solitary lymph follicle.

FIG 6—Case 3. Lymphosarcoma of the jejunum. Very cellular tumor invading the bowel wall. Cells are round, cytoplasm delicate and small in amount.

pathology or to pressure from without. The ureters were not blocked. The psoas shadows were normal. Nothing else of importance was noted.

Comment. There was a definite pyelectasis on the right which evidently indicates some interference with the emptying of the pelvis. There was a little narrowing at the junction of the pelvis with the ureter which may be due to adhesions in this area or to pressure from without.

A film was made with the patient upright and a lead marker was placed over the tumor mass that could be palpated. This mass was quite freely movable. At times it was found in the upper right quadrant while at other times it descended low into the pelvis. It was at first thought that this was connected with the kidney but this film showed that the tumor mass was well below the pelvis of the kidney.

Operation—August 26, 1941. The abdomen was opened through a paramedian incision. There was a tumor about 8 to 10 cm in diameter, originating in the jejunum, about 50 cm below the ligament of Treitz. There was a second smaller tumor about 8 to 10 cm further down in the jejunum. The nodes in the mesentery were all enlarged. There was no evidence of any metastasis to the liver or spleen and the tumor was not adherent. Approximately 68 cm of the jejunum was removed, taking out with this as much of the mesentery as possible, due care being taken not to interfere with larger branches of the superior mesenteric artery. A side-to-side isoperistaltic anastomosis was performed.

Thorough exploration of the abdomen failed to reveal any other pathology. Eight Gm of powdered sulfanilamide was introduced into the abdomen and the wound closed in layers without drainage.

Pathologic Examination—Gross. Dr. E. S. Greenwood. Specimen consisted of two and a half feet of small intestine. In the central portion of the specimen were two large tumor masses, the larger one measuring 8 cm in width and 4.5 cm in depth, and extending clear around the circumference of the intestine. The smaller one was likewise circumferential and measured 3.5 cm in width and 2 cm in depth. The entire intestinal mucosa was studded uniformly with minute miliary tumors, measuring on an average 1 mm in diameter, which were situated beneath the thinned-out mucosa. The large tumor masses were partially ulcerated but they also extended through and beyond the intestinal wall. On cut section the tumor tissue was soft, white and densely cellular in appearance, and scattered throughout were areas of hemorrhage and necrosis. Surrounding both tumors in the mesenteric adipose tissue were many large lymph nodes, measuring up to 3.5 cm in diameter. These lymph nodes were dense white and cellular and on cut section resembled the tumor tissue (Fig. 5).

Microscopically, the sections through each of the large tumor masses and through the large lymph nodes had the structure of a lymphosarcoma. In the two intestinal tumors the neoplastic masses appeared to have originated in the mucosal lymph follicles. In areas the mucosal epithelium and villi still covered the mass, in other areas only remnants of glands remained on the surface and over large areas the surface had ulcerated, apparently from pressure of the mass. At the edges of the tumor the neoplasm was confined to mucosa and submucosa, however, at the center the neoplastic cells had definitely invaded the muscularis and serosa. In the lymph nodes the cells had invaded the capsule and surrounding adipose tissue.

The tumor cells resembled lymphoblasts. They were variable in amount of cytoplasm, size and shape and staining. Mitotic figures were present in small numbers. There were areas in which the cells were pyknotic and necrotic. The entire mucosa of the intestine was fairly heavily infiltrated with lymphocytic cells resembling those found in the tumor masses (Fig. 6). Now and then, in addition, there were lymph follicles (visible grossly).

Sections of the mesenteric nodes showed the structure of the node still present, with germinal follicles in many areas. Here, in addition to altered lymph cells, there were active proliferation of the reticular cells and dilatation of the lymph spaces. *Pathologic Diagnosis*—Jejunum. Lymphosarcoma, generalized with two large tumor masses as well. Mesenteric lymph nodes. Involved in lymphosarcoma.

This patient made an excellent recovery and left the hospital in 12 days following his operation. He was readmitted, September 19, 1941, at which time a roentgenogram of the chest failed to reveal any evidence of metastasis or pulmonary disease. He was given roentgenotherapy through one large anterior portal extending from the xiphoid to

the symphysis. The total dosage was 2,400 r, the target 50 cm from the skin, and the filtration 1 Mm of aluminum and 0.5 Mm of copper. A report from his family physician stated that he died of his disease six weeks after arriving home.

FIG 7

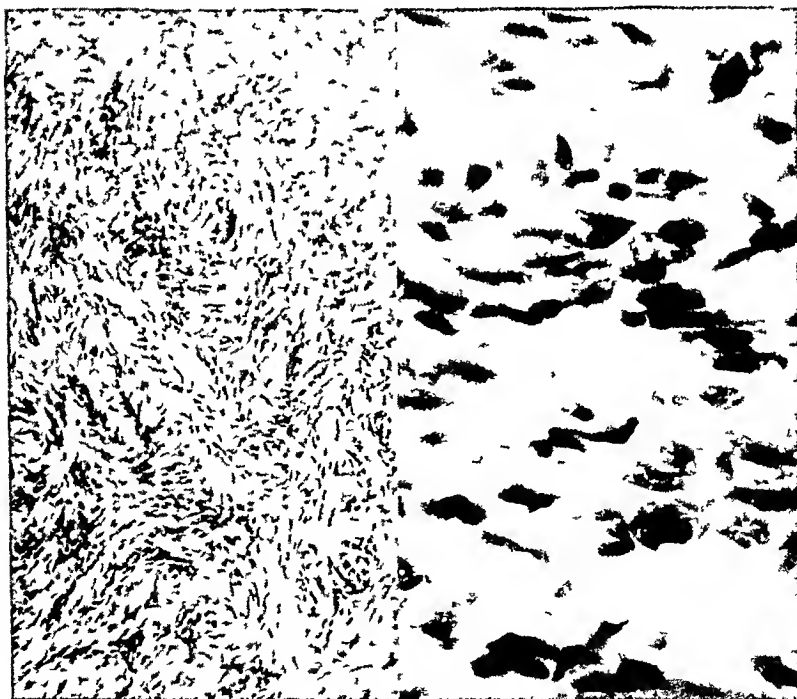
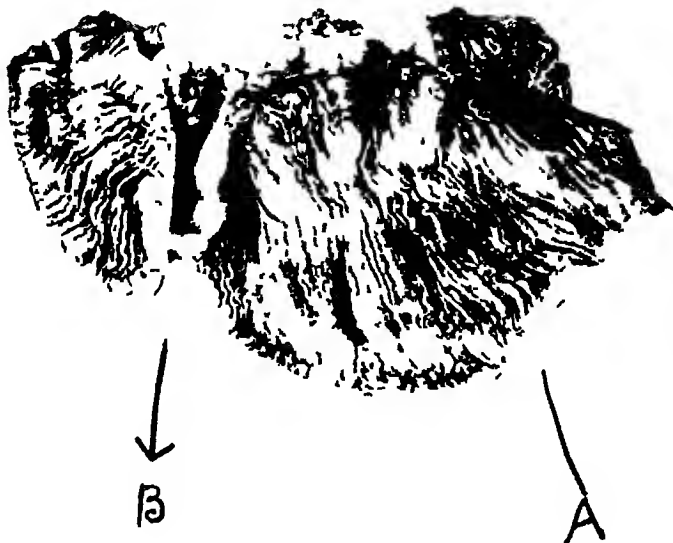


FIG 8

FIG 7—Case 4—Neurofibrosarcoma of jejunum. (A) Shows marked dilatation of proximal loop. (B) Shows tumor of annular constricting type.

FIG 8—Case 4. Neurofibrosarcoma of jejunum. Cells are arranged into bundles and whorls. Nuclei are elongated, cytoplasm abundant but has in distinct boundary.

Case 4—Case No 10835. V. C., white, female, age 14, was admitted to the Louisville City Hospital, January 27, 1941, with history of having had "flu" one month pre-

viously During this attack she vomited two to three times daily All symptoms of the "flu" subsided but the girl continued to vomit, and for two weeks previous to admission she had vomited everything taken by mouth This was unaccompanied by any nausea, and usually occurred 15 to 20 minutes after eating It was not projectile, and had never contained blood She had never noticed any blood in the feces She lost about 28 pounds since the beginning of illness Past and family histories were negative

Physical Examination—Temperature 98° F, pulse 90, respiration 20, blood pressure 106/72 The patient appeared dehydrated, but was otherwise objectively negative

Laboratory Data R B C 5,200,000, hemoglobin 14.5 Gm, W B C 12,000, polys 79%, lymphocytes 18%, monocytes 3% Urinalysis negative Blood Kahn and spinal fluid Kahn negative Spinal tap negative

Roentgenologic examination showed no evidence of free air under diaphragm There was an average amount of gaseous retention in the gastro-intestinal tract Several fluid levels, apparently in the colon, were noted One fluid level was probably in the distal part of the ileum It is not certain that this represents intestinal obstruction Barium enema revealed a dilated and atonic colon There were a few diverticula in the region of splenic flexure The contour of terminal ileum was slightly irregular There was a large round diverticulum with narrow opening about 2 cm proximal to ileocecal valve

An upper gastro-intestinal study was made February 7, 1941 This revealed a 50 per cent retention of barium in the stomach In 24 hours, 30 per cent of the barium remained in the stomach and only a small amount was in the colon

It was thought that the patient had an obstruction of the small bowel The exact location is difficult to determine March 5, 1941, a reexamination of the upper gastro-intestinal tract revealed the jejunum to be markedly dilated There was an obstruction apparently in the jejunum which was much more evident than at the previous examination

Operation—Dr Arnold Griswold A side-to-side anastomosis was made around the tumor mass in the jejunum which was located 18 inches distal to the ligament of Treitz Tumor grossly resembled a scirrhous type of tumor similar to carcinoma of the sigmoid

Three weeks later the tumor and anastomosis were excised and an end-to-end anastomosis of the jejunum carried out, using the Furniss-Clute clamp

Pathologic Examination—The segment of jejunum measured 50 cm in length Near the midpoint was a firm constriction 3.5 cm in length and formed by firm, light-colored tumor tissue which had partly destroyed the wall and constricted the lumen to a few millimeters There was no ulceration The bowel proximal to the constriction was dilated to 5 cm in diameter, its wall markedly thickened by hypertrophy of the muscle coat Below the obstruction the bowel lumen was 3 cm in diameter and the wall normal The mesenteric lymph nodes were moderately enlarged

Sections revealed the tumor to be located in the submucosa chiefly, but it was invading the circular muscle coat and the mucosa Cells were arranged in irregular interlacing strands and bundles Nuclei were fusiform, most having a stippled chromatin pattern, but some were hyperchromatic Morphology was quite uniform and no mitoses were noted The cytoplasm was not abundant and had many fibrillar processes The tumor had replaced the submucosa and much of the mucosa but only slightly damaged the muscle coat The infiltrative type of growth and destruction of tissue were the only definite signs of malignancy There were no metastases in the lymph nodes *Pathologic Diagnosis* Neurofibrosarcoma of the jejunum, obstructing

SUMMARY

All cases of sarcoma of the small intestine that have appeared in the literature since January, 1932, have been reviewed and are listed in the bibliography

Four additional cases are reported, and the symptoms, pathology and treatment of small intestinal sarcoma are discussed

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DISCUSSION —DR L WALLACE FRANK (Louisville, Ky) I have only one thing to add In 1939, we reported two cases of neurofibrosarcomata of the small intestine I believe that within the next few years there will be a change in our conception of the pathology of small intestinal sarcomata, and that many now considered leiomyosarcomata or spindle cell sarcomata will be diagnosed as neurofibrosarcomata

EXTENSION OF THE BORDER LINE OF OPERABILITY IN CANCER OF THE RECTUM*

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AND

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STARTING with the premise that operative removal of cancer of the rectum is at present the best means of effecting a long-term cure, it is obvious that the broader the indications for operation are extended, with reasonable safety, the more patients will ultimately survive. Contrariwise, it is also clear that careful selection of patients for radical operation will mean a low resectability rate, a low mortality rate, a long survival rate, but, of real consequence, only a limited number of patients given a chance to get well. The problem to be discussed is concerned with the limits of operability.

TABLE I

CAUSES OF QUESTIONABLE OPERABILITY IN 105 PATIENTS

	No of Cases
Over 65 years of age	38
One or two nodules in the liver	15
Adiposity	10
Obliterative pelvic peritonitis	9
Resection of prostate or urethra with the rectum	7
Resection of rectovaginal septum with the rectum	6
Peritoneal plaques over the tumor	5
Diabetes	5
Removal of all or part of uterus or adnexa	4
Adherent to prostate (removal capsule)	4
Adherent to bladder	4
Adherent to rectovaginal septum	6
Adherent to sacrum	4
Adherent to uterus	1
Resection of another loop of bowel	1
Marked coronary disease	2
Pregnancy	2
Removal of local recurrence	3
Fixed to abdominal wall	2
Asthma and bronchiectasis	1
Involvement of inguinal nodes	2
Double carcinoma of the rectum	1
Involvement of rectal fistula by adenocarcinoma of rectum	1
Total	133

During the last ten years we have been undertaking radical operations for cancer of the rectum in patients who formerly were considered inoperable due to age, adiposity, attachment of the tumor to surrounding parts, and other

* Read before the Southern Surgical Association, Pinehurst, N C, December 9-11, 1941

factors to be discussed During this period, from 1930 to August, 1941, we have had 277 patients come to the Presbyterian Hospital, on our service, for operation Not included in this study are those patients seen in consultation, some operable, some inoperable, who either refused operation or went elsewhere Of the 277 patients coming in for operation, five were deemed inoperable because of the local fixation or involvement of unremovable tissue In 179 patients the tumor was removed, with an operability rate of 65.8 per cent, and a hospital mortality rate of 7.2 per cent Of these 179 patients, there were 129 one-stage abdominoperineal resections, with a mortality rate of 13, or 10 per cent, 28 two-stage Mummery operations, 16 obstruction resections at the rectosigmoid, five local removals of small tumors, and one resection at the peritoneal reflection, with no deaths Of the 93 inoperable lesions, 84 patients were given a colostomy, with two deaths The causes of inoperability were, namely, liver metastases, fixation of the tumor to the base of the bladder, or extensive involvement of the prostate, vagina or sacrum

If we divide the 179 radical resections into a group of 74 favorable cases, with no question of resectability, and another group of 105 having one or more doubtful factors which clouded resectability, we find the postoperative mortality 4.3 per cent in the first group, and 9.5 per cent in the doubtful group As all of the operative mortality was in the one-stage abdominoperineal group, the mortality in the favorable cases (53) was 5.7 per cent and 13 per cent in the doubtful group (76)

Old age is, and should be, considered as a doubtful factor in operability There was only one patient refused operative treatment because of age He was 81 years old, very feeble, and suffering with chronic bronchitis, and he was simply colostomized Of the 179 patients having operative removal of the tumor, there were 38 patients over 65 years of age, which was the arbitrary age chosen as adding a hazard to the operation, as 28 patients between 60 and 65 went through the operation without much difference in mortality rate from the younger age-group In the 38 patients over 65, there were 18 between 65 and 70 years of age, 12 between 70 and 75, four between 75 and 80, and four between 80 and 85 There were four deaths, or 10.6 per cent operative mortality, in this group, the deaths being from embolism in two and pneumonia in two

TABLE II
AGE AND RADICAL OPERATION FOR CANCER OF THE RECTUM

18 patients between 65-70 years	1 death—embolism
12 patients between 70-75 years	1 death—embolism
4 patients between 75-80 years	1 death—pneumonia
4 patients between 80-85 years	1 death—pneumonia
—	—
38 patients over 65 years	4 deaths (10.6 per cent)

The choice of operation in this age-group was somewhat different than in patients under 65, in whom we almost always use the one-stage abdominoperineal operation Twenty-two patients had a one-stage abdominoperineal resection with four deaths, or 18.2 per cent, seven patients had a two-stage

Mummery operation, three an obstruction resection operation for a lesion at the rectosigmoid, and three a local removal of the tumor, the latter groups with no mortality

Even though the operative risk in this group of patients has been high, we feel sure that we have given years of life expectancy to a considerable group. Of nine patients over 65 years of age operated upon more than five years ago, five lived over five years. Of four patients of this group operated upon more than four years ago, two lived over four years. In other words, age rarely should be considered a contraindication to operative removal of the tumor.

One of the most difficult decisions to make in favor of radical removal of the tumor is in patients where the tumor is adherent to structures outside the bowel. As already indicated, we found a relatively large number of patients inoperable for this reason, but in the past five years we have become more radical and have resected a large part of the prostate in five patients, the rectovaginal septum in six, the uterus and adnexa in four, the ureter in two, the dome and posterior half of the bladder in one, and another loop of bowel in one. There were two postoperative deaths in this group, one from pneumonia and one from sepsis. Sufficient time has not passed to speak with authority on the long-term cure of these patients but our impression is, from a review of the follow-up, that a considerable number will be given a three- to five-year cure.

There is an added group of 21 patients where the tumor was attached, but not necessarily by infiltration, where part of the prostate (six), the periosteum of the sacrum (five), a portion of the base of the bladder (four), rectovaginal septum (five), or uterus (one), was removed. Of this group there was one postoperative death from peritonitis due to the fact that the tumor had perforated into the hollow of the sacrum. There have been five local recurrences of the growth, and the most unfavorable are those where the tumor is attached to the sacrum. Of the whole group, two are living and well after three years, and four have lived over five years.

There have been 15 patients with one or two small nodules in the liver at the time of operation who have been given the benefit of a radical removal of the tumor. We have not been impressed with the soundness of undertaking radical operations where definite liver involvement is present, due to the tedious convalescence following radical operation coupled with an average expectancy of only ten months in any patient having definite liver involvement at the time of operation. The presence of one or more small nodules in the liver presents an entirely different problem, as the differential diagnosis between early carcinoma of the liver and an adenoma or angioma is very difficult to make by touch. Of the 15 patients in this latter group, four have had recurrence in the liver and have died on an average of ten months postoperatively. Four of these patients are alive three to five years postoperatively, which justifies giving patients with questionable lesions in the liver an operative chance of cure.

Adiposity has not been considered a contraindication to operation in any

patient, although the added risk of intra-abdominal procedures in fat patients is well known. There were ten patients in this group who were exceedingly fat, most of them rather short with large abdomens. There was one postoperative death from embolism and one evisceration which was repaired and from which the patient recovered. Eight patients had one-stage abdominoperineal resections, one a two-stage Mummery operation, and one other a resection of the tumor with closure of the distal rectal segment of the bowel. In the follow-up, two patients died within a year of liver metastases, one of these having had a nodule in the liver at the time of operation. The other seven patients are alive, one five years, two three years, and two two years postoperatively. In operating upon such a group, the surgeon must be prepared for poor exposure of the operative field and a willingness to do much of the dissection by touch. There is, no doubt, an added risk of hemorrhage, infection, evisceration, and cardiovascular accidents. In spite of these dangers there is 100 per cent expectancy of death if no operation is done, and that is the impelling indication for operation in all increased risk patients with carcinoma of the rectum.

In nine patients having a radical removal of the tumor there was an obliterative peritonitis of the small pelvis resulting from a previous operation or due to endometriosis or diverticulitis. This complication is an annoying and somewhat dangerous one in that an hour's time may be necessary for obtaining proper exposure in some of these patients, and the danger of peritonitis by getting into the bowel or tumor is always present. One of these patients died of sepsis due to inadvertent cutting of a ureter.

Four patients were found to have a perforation of the tumor with local abscess formation at the time of operation. The soft-part inflammatory mass was removed with the tumor. One of these patients died of postoperative peritonitis. The other three are still alive three to five years after operation.

Among the miscellaneous factors making operability somewhat doubtful were peritoneal plaques over the tumor (five), diabetes (five), pregnancy (two), removal of local recurrences (three), marked symptoms from coronary disease (two), fixation of the tumor to the abdominal wall (two), ulcerative colitis (one), asthma and bronchiectasis (one), involvement of inguinal nodes (two), double carcinoma of the rectum (one), and involvement of an extensive rectal fistula with transplanted cancer from an adenocarcinoma of the ampulla (one). Of this group there was one postoperative death from peritonitis in a patient with peritoneal plaques over the tumor, the cause of the peritonitis was unknown. The most unfavorable group was five patients having peritoneal plaques over the tumor. In addition to the postoperative death mentioned, three had recurrences in the peritoneum within two years, one patient is living six years after operation.

Of the 105 patients classed as being doubtfully operable, there were 18 having more than one factor influencing that decision. Of that group, there were two hospital deaths.

No previous mention has been made of lymph node involvement as a

contraindication to operative removal of the tumor for the reason that gross enlargement of the nodes may be due to infection. Knowing that 65 per cent of lymph nodes are involved with carcinoma at the time of operation and that many nodes are involved that cannot be determined by palpation alone, we have favored the one-stage abdominoperineal operation as offering the best opportunity of widespread removal of the lymphatic tissue draining the rectum.

TABLE III
OPERABILITY

	To August 1941	1940	1939	1938	1937	1936	1935	1934	1933	1932	1931	To- tal
Total operated upon	26	35	36	33	41	30	18	12	16	14	16	277
<i>Radical Resection</i>	17	24	24	24	27	19	12	6	7	9	10	179
Abdominoperineal resection	16	22	18	18	25	15	8	2	4		1	129
Mummery—2 stage			1	1	1	2	4	4	2	7	6	28
Obstruction resection	1	1	4	4	1	2				1	2	16
Local removal		1	1						1	1	1	5
Resection				1								1
<i>Inoperable</i>	9	11	12	9	14	11	6	6	9	5	6	98
Colostomy	8	10	12	3	13	10	5	5	8	5	5	84
Nothing done	1	1		6	1	1	1	1	1		1	14
<i>Questionable Operability</i>	13	13	21	14	15	9	7	3	4	5	1	105
Abdominoperineal resection	12	11	16	10	15	7	3	1	3			78
Mummery—2 stage			1	1		2	4	2	1	4	1	16
Obstruction resection	1	1	3	2								7
Local removal		1	1							1		3
Resection				1								1

In this report we have discussed a group of patients with cancer of the rectum having one or more factors which increase the hazards of operation and in some instances, without doubt, decrease the chances of long-term survival. It is our belief that the indications for operation should be broadened as long as the mortality rate can be kept within reasonable bounds and the long survival rate reasonably high. It is hoped that the experience of others in this doubtful class of patients may be recorded so that the limits of operability may be more clearly defined.

DISCUSSION —DR FRED W. RANKIN (Lexington, Ky.) This is such an excellent piece of work which Doctor David has presented that I feel one should probably congratulate him on the presentation and not attempt to discuss it, for there are so many points which need attention, and time is too short to take them up in order. It must be digested in its published form to be fully appreciated. He has gone into the question of operability of cancer of the rectum in a most meticulous manner. He has discussed the extension of the horizon of operability to the point of removal of portions of adjacent viscera, including loops of small bowel, and I am entirely in accord with his thesis. Likewise, I agree with him that the cases which have plaques of carcinoma on the pelvic peritoneum have a particularly poor prognosis, but still I feel that they should be resected, removing all visible plaques. When one is confronted with the question of cancer of the liver in an otherwise operable rectal cancer, the decision is not so simple and easy. The operation is formidable even in the hands of expert surgeons, and the convalescence is long, the metastases have undermined the resistance of the patient and the

mortality rate is bound to be higher. On the other hand, a death from liver cancer is much more comfortable than one from an obstructing, locally spreading rectal cancer. Undoubtedly, a resection operation in the presence of liver metastasis is frequently justified, but, certainly, it should not be made routine. Occasionally, following such an operation, we are surprised by a duration of life of more than ten or 12 months.

Doctor David, two or three years ago, presented before the American Surgical Association his work on lymph node involvement in cancer of the rectum, which, to my mind, was clinching evidence—if any more argument is needed than clinical experience—that the radical procedure for cancer of the rectum, doing it in one stage, will unquestionably give the most satisfactory end-result. I believe that his demonstration, which showed that the more nodes examined, the more were found to be involved, is a monument of industry, and eliminates, completely, any arguments for local excision of rectal cancer with reestablishment of the bowel lumen, save in a very small group of cases. With 65 per cent or more of involved nodes in cancer of the rectum, there is no question of the futility of these local operations, and they should not be employed save only in cases where any other kind of operation is impossible because of coexisting debilitating disease or local conditions. Doctor David's work on lymph node involvement in cancer of the rectum, to my mind, is one of the most outstanding pieces of work which has ever been done on this disease in this country.

With the extension of operability, obviously, the mortality must be kept within reasonable bounds, the question is, what are reasonable bounds? A mortality, following resection, of less than 10 per cent, is certainly reasonable, and Doctor David has shown that with proper teamwork, proper preoperative care and postoperative observation, the mortality figure can be kept between 5 and 10 per cent. His figures of 4 and 9.3 per cent in the favorable and unfavorable groups are eminently satisfactory, and I think are not likely to be improved upon.

I want to congratulate him on this magnificent paper, and to agree with him that the resectability rate, which permits the removal of 80 or more cancers out of 100, as they come into the clinic, is a distinct advance and will improve the figures on longevity.

DR HARVEY STONE (Baltimore, Md.) I agree with what Doctor Rankin and Doctor David have said. In the present stage of surgical treatment in this condition, the type of operation is preferably the one-stage abdominoperineal resection, of the general kind advocated by Miles. I do not think there is much difference of opinion on that point. However, as I listened to Doctor David, it seemed to me that his principal thesis was not concerned with the kind of operation but with the problem of when operation should be performed. In other words, under what circumstances should one undertake radical surgery for this condition?

I was particularly glad to hear his paper and Doctor Rankin's discussion, because I find myself in a most unsatisfactory position on this question. I go through cycles. I fully agree with the principle that the only present method of curing the disease is by widespread radical surgery, and on that basis I think every extension, within reason, of criteria of operability is a step in the right direction. But what happens is this. I proceed on that basis, and in a few cases will include a little more, and a little more, in the scope of operability, and feel satisfied until I run into three or four cases in which I operate in doubtful circumstances and something goes wrong. I have had two or three deaths, or a series of distressing prolonged convalescences, with the

patient probably dying after five or six months with the original disease, and that sets me back on my heels. I begin to wonder whether I exercised rational judgment and I begin to swing back. I confess it is highly confusing. In principle, I fully agree that the extension of operability should be widened, but, in practice, I confess that after running into trouble my knees weaken and I begin to shrink back.

DR WILLIAM MARBURY (Washington, D. C.) I shall not attempt to comment on Doctor David's paper directly—which has been so ably done by Doctor Rankin and Doctor Stone—but I want to mention a colostomy tube used for cleaning out the left side of the colon. This is more applicable for obstructive growths in the sigmoid, but applies to those in the rectosigmoid region also. The tube is a double lumen tube, on the order of that of Miller-Abbott, but is about the size of a stomach tube. It is passed into the bowel through a cecostomy and gradually worked around to the descending colon. The difficulty is to make it pass the splenic flexure (Fig. 1), and this is facilitated by putting the patient in the Trendelenburg position.



FIG. 1—Roentgenogram showing the colostomy tube traversing the entire colon down to the obstruction. Barium enema extends up to the obstruction.

We thought that if it were possible to clean out the left side of the colon, a one-stage resection would be made much safer. I think we have all found the colon so full of feces in these obstructed cases that a primary resection was ill-advised. In some of the large clinics a primary resection has been abandoned for a modified Mikulicz's. The mechanical part has worked out satisfactorily in a few cases, but we have not as yet been able to liquefy the feces in the descending colon so as properly to clean it out. Some experiments are being undertaken to accomplish this if possible.

The slide shows the tube extending from the cecostomy to the obstruction in the sigmoid.

DR VERNON C. DAVID (Chicago, Ill., closing) I once did most operations of this type at Cook County Hospital, and there our operability rate was much lower, as I think it is in all charity hospitals, than in private practice. Therefore, any fig-

ure as to operability rate must concern many other things.

The remarks of Doctor Rankin about cancer of the rectum come, of course, from an authority who has had no small part in making operation in this field successful, because, from the start, he has been an advocate of widespread radical surgery. He has also given us indications for operation in early cases, allowing one to perform resection with eventual closure in a two- or three-stage operation. For that reason his contributions and those of Doctor Stone, and many others, have more and more increased the element of safety.

Doctor Stone brought out a very human side of the discussion, which I

think affects us all, but as surgeons we must have broad backs. When we are faced with 100 per cent loss of patients if the lesion is not removed, I think we all feel better in our minds about giving doubtful cases a chance. I think the larger the indications for operation become, the higher will be the mortality of the operation, but if, at the end of a given time, we have more patients alive, we can certainly feel happy about extending the operability. To lose two or three patients does change one's philosophy, but if, over a period of time, we can show our mortality figures still low, and the range of operability higher, then I think we can say we are on firm ground.

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ANNULAR PANCREAS AS A CLINICAL PROBLEM*

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ANNULAR PANCREAS is an anatomic anomaly of great rarity. The reports of only 48 cases have been found in the anatomic, pathologic and surgical literature and of these only ten cases have been operated upon. The condition presents, therefore, one of the most unusual of clinical problems, the surgical relationships of which are entirely undefined. In no previous case has the diagnosis been suggested preoperatively and there is no agreement on surgical treatment. The present report deals with a single treated case with a correct tentative preoperative diagnosis. The clinical implications of the condition will be stressed.

Case Report—Hospital No 155428 B R, white, male, age 23, unmarried, was admitted to the hospital, February 2, 1940, following study in the Out-Patient Department, where he was first seen eight months previously. The patient is an underdeveloped young white man of illiterate rural stock who is obviously ignorant and of low grade mentality. His IQ, on the revised Stanford-Binet Intelligence Scale, is within the range of the low moron, and he can neither read nor write, having gone no further in school than the first grade. The many histories obtained during observation are, therefore, variable and unreliable. In general, the complaint seems to be that of sharply limited non-radiating epigastric pain, occurring in attacks of irregular frequency. At times the attacks were at intervals of a month and at other times occurred several times a day. They were apparently not associated with meals, but the patient felt that eating increased the pain and had, therefore, limited his diet. The pain was agonizing in severity, so that his family physician gave him morphine for relief on many occasions. Apparently the drug was employed quite freely without regard to possible habit formation. Belladonna and alkalies had no effect on the pain. There was no known fever with the attacks, and, until just before admission to the hospital, no vomiting. There were no other abdominal symptoms, no disturbances of bowel function, and no abnormal stools. The original Out-Patient diagnosis was pylorospasm and peptic ulcer.

The first roentgenologic examination, November 21, 1939, showed "On ingestion of the barium meal the esophagus was negative. The stomach filled readily, and except for a somewhat excessive degree of spasticity in the prepyloric area, it appeared within the limits of normal. The proximal portion of the duodenum was seen to dilate as the barium flowed in. This dilatation ended abruptly in the second portion of the duodenum where the barium passed an oval defect two centimeters in diameter in a narrow stream (Fig 1). The duodenum in this area was not fixed and the defect was within the lumen. Distal to this, and up to the ligament of Treitz, the duodenum was somewhat dilated and there was a slight delay in the passage of barium at the ligament. This distal portion of the duodenum had a somewhat ragged appearance which is not believed to be of clinical significance since this portion was freely movable and the wall seemed pliable. At six hours there was about a five per cent gastric residue and there was a little barium in the duodenum outlining the defect seen at the first examination. The head of the meal was still in the small intestine. At 24 hours the ascending and the descending colons were fairly well outlined and appeared grossly negative. *Roentgenologic Conclusions* Polyp, two centimeters in diameter, in the second portion of the duodenum, most probably benign. Low-grade obstruction at the ligament of Treitz."

* Read before the Southern Surgical Association, Pinehurst, N C, December 9-11, 1941

Just before admission to the hospital the patient had a much more severe attack of pain, with vomiting, and again received hypodermics of morphine. The abdominal examination was negative except for slight epigastric tenderness. The results of the usual laboratory examinations, including the Wassermann and Kahn reactions in the blood, were normal. There was no anemia. A review of the roentgenograms resulted in an opinion that the lesion observed in the duodenum was more probably a constricting ulcer than a polyp.



FIG 1—Roentgenogram of case of annular pancreas. Note smooth filling defect (between arrows) in dextral aspect of second portion of duodenum.

On account of the smooth contour of the defect (Fig 1) the surgeon suggested the diagnosis of annular pancreas and the case was presented before a staff conference with emphasis on this diagnosis as a possibility.

Operation—Under spinal anesthesia, a transverse upper abdominal incision was made. The gallbladder was normal, as was the liver. The appendix was not seen. No pathologic findings were noted with the exception of those in the duodenum and pancreas. The dilated first portion of the duodenum was readily identified and the duodenum was mobilized by an incision in the peritoneum at the outer side. Palpation of the pancreas then revealed a diffuse nodular enlargement of the organ. In the head of the pancreas the nodules were large and hard and suggested malignancy. The tail of the pancreas was also indurated and enlarged so that its cross-section was nearly circular. During this phase of dissection and examination the site of obstruction was not obvious. It was felt that if the obstruction were due to tumor, further surgery might not be justified. One of the nodules in the head of the pancreas was, therefore, approached from beneath, and a specimen about one centimeter in diameter was obtained. A duct was opened, from which clear fluid escaped, presumably pancreatic juice. The wound in the pancreas was closed with two layers of fine silk sutures. Pending the report of a frozen section, a further search was made in the region of the obstruction. The diagnosis of annular pancreas then became clear (Fig 2). In the lowest part of the second portion of the duodenum there could be seen what was apparently pancreatic tissue in a band stretching across the duodenum. On the superior surface this band was about three centimeters in diameter and narrowed to about 1.5 centimeters in diameter at the under surface where it disappeared beneath the duodenum. Superficially it appeared thin but after dissection it proved to be about one centimeter in thickness. A plane of cleavage

between this structure and the duodenum was found and it was then divided. Immediately the duodenum unfolded to an extent of about four centimeters, with apparently complete relief of the obstruction (Fig 3). About one centimeter of the anterior portion of the ring was further dissected off the duodenum and removed for biopsy. The cut ends of the pancreatic ring were closed with mattress sutures of fine silk. The duodenum was then dropped back in place and the abdominal wound was closed with interrupted sutures of fine braided silk in layers.



FIG 2—Sketch of operative findings in case of annular pancreas

Pathology—The frozen section from the head of the pancreas showed inflammation and fibrosis. The report by Dr J R Cash from the excised segment of the ring is as follows: "A section through the main mass shows a large duct with many small surrounding tributaries, all lined by columnar epithelium. Three smaller, similar ducts, which may well be main branches of the large duct, are also present. All of these ducts are embedded in dense fibrous tissue. Closely adjacent to them are several intact unaltered nodules of pancreatic tissue in which a number of small, but quite typical islands of Langerhans are seen. Embedded in other areas of the fibrous tissue are scattered islands of Langerhans. These vary from about normal size to small groups containing only five or six islet cells. The fibrous tissue is fairly rich in blood vessels and contains a number of small nerve trunks. In this section there is only very slight perivascular and periductal infiltration by lymphocytes. Several small fragments of tissue from the head of the pancreas, of which frozen sections had been made, show a few small ducts similar to those just described, and scattered islands of Langerhans embedded in fibrous tissue and fat. Occasional small groups of acinar cells are also seen. Of special interest in these latter sections is the presence of many more lymphocytes about the blood vessels and ducts as well as quite extensive and diffuse infiltration of all of the tissue with polymorphonuclear neutrophils and leukocytes and numerous monocytes. No evidence of fat necrosis is seen. *Pathologic Diagnosis* Atrophic pancreatic tissue showing long-standing subacute inflammation" (Fig 4).

Postoperative Course—The patient had a smooth immediate recovery and was discharged on the eleventh day, apparently well, with the wound cleanly healed. He was readmitted on the seventeenth postoperative day with recurrence of his epigastric pain, now radiating around the right side of the back, for which he had again received hypodermic injections. On this occasion the temperature was 99.2°F , the leukocyte count was 18,000, and there was definite tenderness in the epigastrium. His complaints were



FIG 3—Same as Figure 2, after division of ring and partial suture of cut ends. Note unfolding of duodenum.

extremely violent at first, but ceased immediately following a hypodermic injection of codeine. The next day he was apparently comfortable and was discharged three days later, without complaints. The blood amylase was 29.4 mg per cent.

The patient continued to return to the Out-Patient Department at frequent intervals, with the same type of complaint. His home physician was giving him morphine whenever he was called. On several occasions in the Out-Patient Department the pain promptly ceased following a hypodermic of sterile water.

On April 11, 1940 a gastro-intestinal roentgenologic examination showed "On ingestion of the barium meal the esophagus was negative. The stomach filled readily. The pylorus was very spastic. The second portion of the duodenum was pulled far to the right, and there was a low-grade obstruction. Otherwise, no definite abnormalities were demonstrated. At six hours the stomach was empty and the head of the meal in the ileum. At 24 hours barium was scattered throughout the large bowel in insufficient quantity to warrant any further opinion. *Roentgenologic Conclusions* Low-grade obstruction in the second portion of the duodenum which is drawn far to the right. Very spastic pylorus." Similar findings were reported in July and August, 1940, and again in January, 1941.

The last recorded visit was on May 18, 1941, on which occasion he was found to

have a urinary retention of 1,000 cc. On this occasion, again, complete relief of pain was immediately obtained following a hypodermic of sterile water.

SUMMARY—Herewith is reported the case of a moronic young man with characteristic symptoms of chronic duodenal obstruction of a year's duration, apparently due to annular pancreas, complicated by chronic interstitial pancreatitis and treated by partial excision of the ring. He had been managed by his home physician with liberal amounts of morphine which, after operation, were continued on any excuse. After discharge the patient had persistent symptoms resembling the original complaint, frequently relieved following a hypodermic of sterile water. Postoperative roentgenologic studies revealed deformity of the duodenum, believed due to adhesions, with slowing of the stream but with no six-hour retention. The patient's mental level, and a probable morphine habituation, make the symptomatic results of the operation impossible to estimate.

Incidence—McNaught,¹⁶ in 1933, presented a thorough review of the literature of annular pancreas, and a table showing the 40 recorded cases (including one of his own), since the condition was first described by Tiedeman, in 1818. In 1935, he and Cox¹⁷ brought the record up to date, with the addition of three cases from the literature, and reported a second case of their own. Since that date, reports of three additional cases^{9, 18, 19} have been found, which, with the case herein described, make a total of 48 cases now on record.

Anatomy—Briefly, the anomaly consists of the prolongation of an annular process from the head of the pancreas to surround the duodenum, which is usually completely embraced by a ring of pancreatic tissue (Fig. 2). If the ring is not complete, the defect occurs on the anterior surface of the duodenum^{13, 15} where the anomalous structure would otherwise fuse with the anterior surface of the head of the pancreas. It differs from most other anomalies of the pancreas in presenting an abnormal structural relationship to the duodenum that is, theoretically and actually, capable of causing mechanical disturbance of the function of the bowel. There is, in fact, in almost all described cases a narrowing of the lumen of the duodenum at the site of the encircling band, and a dilatation of the bowel above the narrow point, the latter often accompanied by thickening of the wall. That this partial duodenal obstruction is apparently not always a cause of symptoms will be emphasized below.

A second point of anatomic importance is the duct structure in the anomalous ring. Except when the subject of pathologic changes common in the anatomically normal pancreas, the ring cannot be distinguished histologically from normal pancreatic tissue, it is obviously an active portion of a secreting gland and possesses a duct system with a principal channel and tributaries comparable to the corresponding structures in the rest of the pancreas. Interest in the anatomy of this duct has been intense, so that many careful studies of its origin and course are available.^{11, 12, 17, 18, 19} All adequately studied specimens have shown a constant anterior point of origin of the duct, which subsequently courses to the right over the duodenum, then posteriorly, then to the left behind the duodenum, and finally enters the head of the pancreas in close relationship to the common duct (Fig. 5). Here it almost always empties into the main pancreatic duct,⁴ but may terminate otherwise.¹⁹ Inter-

est in the duct has been centered entirely on the attempt to find an embryologic explanation for the anomaly. It will be pointed out that the anatomy of the duct has surgical importance.

Embryology—The embryologic origin of annular pancreas had been adequately discussed both in the American and foreign literature. Although there is some disagreement, the majority opinion among later writers holds, with Lecco,¹⁰ that the anomaly occurs as the result of a failure of complete migration of the ventral anlage of the gland, the tip of which remains in an anterior position while the duct outlet into the bowel rotates to the right and posteriorly.



FIG. 4.—Section from biopsy of pancreatic ring showing duct and islands surrounded by fibrous tissue and a small segment of relatively normal acinar tissue.

in the normal manner to become the distal portion of the duct of Winsung. There is thus left behind a strip of pancreatic tissue encircling the duodenum. The point of origin of the annular duct, its usual outlet into the duct of Winsung, and the occasional anterior defect in the ring all tend to support this hypothesis. The reader is referred to McNaught's excellent description¹⁶ for a more detailed consideration.

Pathology—In addition to the obstruction of the duodenum already mentioned as a part of the gross anatomy of the anomaly, associated pathologic changes may be divided into two categories. Those in the anomalous structure itself, and those elsewhere. Although in some cases^{14, 15, 17, 4} (Cases 1 and 2) the annular portion of the pancreas presents no pathologic change, the incidence of chronic interstitial pancreatitis is rather higher than one would expect. The fact that the ring was found to be diseased in all five cases operated upon in which microscopic study of the tissue is reported (Table I) suggests the possible relationship of inflammatory changes in the ring to the development of clinical symptoms, as has been pointed out by others^{5, 7, 16}. The rigidity of the inflammatory tissue is an adequate explanation for the

TABLE I
ANALYSIS OF TEN CASES OF ANNULAR PANCREAS TREATED BY SURGICAL OPERATION

Case No	Reported by	Sex Age	Clinical Picture	X ray	Proper Diagnosis	Diag. At Oper Table	Operation	Path of Interest	Result	Remarks
1	Vidal ¹ 1905	Male 3 days	Congenital pyloric or duodenal obstruction	None	Congential high obstruction	Annular pancreas	Post gastro enterostomy	No report	Cure	Also congenital atresia of duodenum
2	dos Santos ² 1906	Female 26 yrs	Duodenal obstruction	None	Pyloric or duodenal obst	Ptosis of stomach	Post gastro enterostomy	Chronic interstitial pancreatitis	Died (pneumonia)	Diagnosis at post-mortem
3	Lerat ³ 1908	Female 46 yrs	Duodenal obstruction	Neg for pancreatic calculi	Chr pancreatitis Cholecystitis Appendicitis	Annular pancreas	Resection of pancreatic ring Cholecystectomy Appendicectomy	Patchy sclerosis about ducts of pancreas	Cure	Drainage ceased on 13th day
4	Smetana ⁴ (Case 3) 1928	Male 74 yrs	Duodenal obstruction	None	Tumor of duodenum	Tumor of duodenum	Post gastro enterostomy	Marked sclerosis of pancreas Superficial ulcers of duodenum Ca of cystic duct	Died several hours after operation	Diagnosis at post-mortem
5	Howard ⁵ 1930	Female 46 yrs	Duodenal obstruction	Diverticulum 2nd portion duodenum	Chronic duodenal ileus	Annular pancreas	Division of ring	No report	Cure complicated by pancreatic fistula	Second operation necessary for drainage
6	Brines ⁶ 1930	Male 35 yrs (Negro)	Acute abdominal emergency 3 days duration	None	Acute abdominal emergency	Retropertoneal hemorrhage	Drainage	Chr interstitial and acute hemorrhagic pancreatitis Chronic cholecystitis	Died 1 1/4 hours after operation	Diagnosis at post-mortem
7	Zech ⁷ 1931	Female 27 yrs	Duodenal obstruction	Partial obstruction duodenum Diminished function gallbladder	Obstruction duodenum from adhesions Cholecystitis	Annular pancreas	Division of ring Hencke-Mikulicz on duodenum Cholecystectomy	No report	Cure (2 years) complicated by small pancreatic fistula	Duodenum did not expand after division of ring
8	Brines ⁸ 1931	Male 44 yrs	Duodenal obstruction	Dilated stomach Deformed bulb Gastric retention	Duodenal ulcer with stenosis	Chronic gastric ulcer	Post gastro enterostomy	No report	Died (respiratory infection)	Diagnosis at post-mortem
9	Truelsen ⁹ 1940	Male 35 yrs	Duodenal obstruction	Duodenal diverticulum	Duodenal diverticulum	Annular pancreas	Post gastro enterostomy Narrowing of 1st portion duodenum by open operation	No report	Cure	Postoperative x-ray Functioning gastro-enterostomy Duodenal ballooning gone
10	Lehman 1942	Male 23 yrs	Duodenal obstruction	Polyp of duodenum or constricting ulcer	Chr duodenal ileus Annular pancreas?	Annular pancreas	Partial resection of ring	Chronic interstitial pancreatitis	Recovery but persistent symptoms	Postoperative x ray Persistent deformity of duodenum

origin of obstructive symptoms In Brines' first case,⁶ of acute hemorrhagic pancreatitis involving the ring, the secondary disease apparently precipitated acute duodenal obstruction

The reason for the occurrence of chronic or acute pancreatitis in a considerable number of instances is not clear It is possible that the theory of Rich and Duff,²⁰ in explanation of the etiology of pancreatic inflammation, may be even more logical in this condition than in the nonanomalous pancreas The pressure behind partially occluded ducts may be exaggerated by the relatively tortuous course of the main duct and by increased intraductal pressure caused by duodenal peristalsis and the crowding of the ballooned duodenum down upon the ring

In the second category, ulceration of the stomach or duodenum has been frequently reported^{2, 8, 4} (Case 2) These are, of course, common enough, in general, to make indefinite any direct association between ulceration and the anomaly It is possible, however, that chronic duodenal obstruction at this level might disturb the acid-base relationships at the pylorus Truelsen⁹ ascribes the occurrence of ulcer to stasis in the stomach and bowel Finally, as with other congenital malformations, annular pancreas is associated with a high incidence of other anatomic anomalies (25 per cent according to McNaught and Cox¹⁷) which need not be listed here

Clinical Picture—It is a striking fact, that of the 48 cases of record, 38 cases are reported only as the result of incidental observations in the pathologic or anatomic laboratories Most of these 38 reports present no or meager clinical data, but several of the observations were made following death from other causes at advanced ages (65,¹⁹ 70,¹⁷ and 74 years,⁴ (Case 2) respectively) McNaught¹⁶ states that the reports of his original series of 40 cases from the literature were accompanied by clinical data in 15 instances, and that of these 15 cases, nine (60 per cent) presented abdominal symptoms in varying degree Among these nine cases, however, are the seven cases that came to operation during this period Although it is obvious that annular pancreas can cause symptoms, these facts lead to the conclusions that the condition is in many instances compatible with long life, and that probably considerably more than one-half of the cases do not present a disturbing degree of illness The possibility that inflammatory changes in the ring may precipitate symptoms has already been referred to

The study of the cases found incidentally after death from other causes, although interesting from the embryologic and pathologic points of view, does not illumine the clinical aspects of the condition as does the study of the ten cases recognized and treated as clinical problems These ten cases, analyzed in Table I, present interesting aspects for discussion

When symptoms occur they are, for the most part, those of duodenal obstruction The picture may be complicated by the presence of the symptoms of an associated ulcer, including hematemesis In one instance⁶ the symptoms were those of an acute abdominal condition, later proven to be acute hemorrhagic pancreatitis involving the ring

Diagnosis—It is obvious that a diagnosis of annular pancreas cannot be made on clinical data alone. Of five cases examined roentgenologically before operation with the use of contrast material (Cases 5, 7, 8, 9, 10), the diagnosis was not made in four by the roentgenologist, and was originally missed in the fifth (Case 10). In view of the roentgenographic appearance of the lesion (Fig 1), it would seem that careful roentgenologic examination of the duodenum in all cases of partial obstruction of the descending portion should permit a presumptive diagnosis in at least some instances, or, if not a presumptive diagnosis, at least the mention of annular pancreas among the etiologic possibilities. The failure to diagnose the disease stems from the failure to consider it, which, in turn, is caused by its apparent extreme rarity.

The diagnostic record of the surgeons who have operated for symptoms arising from the disease is not good. In three out of ten cases (Table I) the surgeons missed the condition at operation, though searching for the cause of obstructive symptoms, and in a fourth, under more difficult circumstances, the operator⁶ recognized only the presence of retroperitoneal hemorrhage. In our personal experience the demonstration of the ring did not occur until considerable dissection in the region of the pancreas and duodenum had been carried out. It is possible that a number of cases have been missed through failure of the surgeon to remember that annular pancreas occurs.

This disease will probably remain difficult to diagnose roentgenologically and to be easily missed on exploration. It is safe to affirm, however, that the syndrome of chronic duodenal ileus, supplemented by corroborative roentgenographic evidence of obstruction, which also reveals a smooth niche constricting the second portion of the duodenum from its dextral aspect, should make possible, at times, a correct preoperative diagnosis. It must be remembered that chronic stenosing ulcer of the descending portion of the duodenum may present roentgenographic appearances indistinguishable from the outline described. Certainly, when operating for chronic duodenal ileus, the surgeon should thoroughly expose the anterior and lateral surfaces of the duodenum as far distally as the beginning of the third portion, mobilizing the transverse colon if necessary.

Treatment—The treatment of the condition, when necessary, is obviously surgical. Two methods of attack seem more or less logical, namely, indirect methods such as posterior gastro-enterostomy or duodenojejunostomy, and direct methods such as division or partial resection of the ring with or without a plastic procedure upon the constricted duodenum. Of these, all but duodenojejunostomy have actually been employed on treated cases (Table I).

The most popular operation has been posterior gastro-enterostomy, the value of which is hard to judge from the results. Of five cases treated by this operation (Cases 1, 2, 4, 8, 9), three died postoperatively from respiratory infections. In one case (Case 1), the most important cause of obstruction was a congenital atresia of the duodenum beginning at the pylorus, for

which gastro-enterostomy is, of course, a logical procedure. The complete recovery in this case is, therefore, no evidence of the value of the operation for obstruction in the second portion of the duodenum. In the fifth instance (Case 9), recovery followed gastro-enterostomy, but here an additional, not particularly logical, procedure was also carried out. The surgeon, having opened the first portion of the duodenum longitudinally in establishing the diagnosis, closed it in the same direction with care to narrow its lumen to a degree approaching the normal.

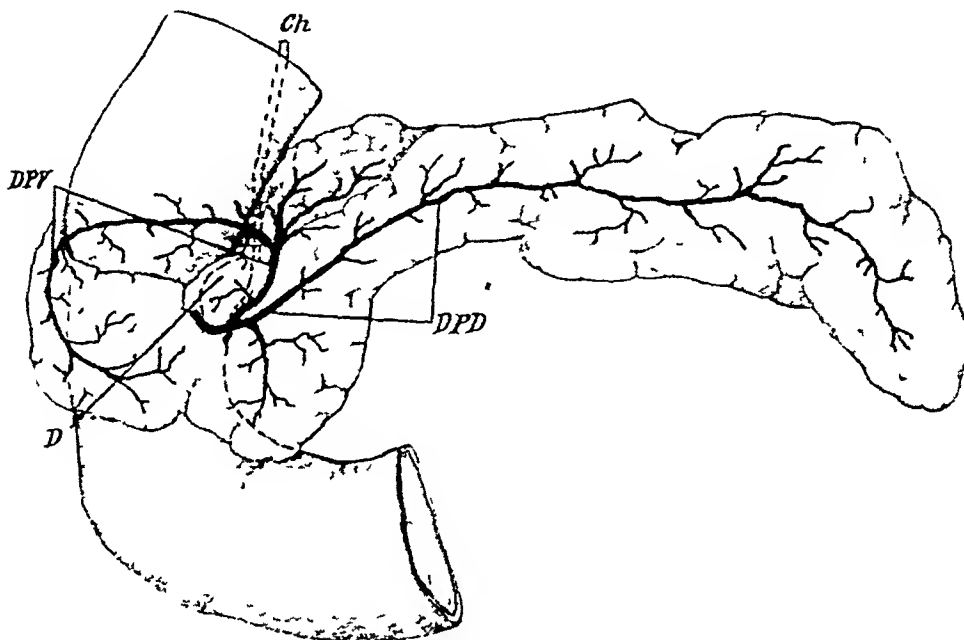


FIG 5—Diagram of typical duct anatomy of annular pancreas (from Cords¹²) The posterior portion of the duct of the ring has been drawn as though it passed anterior to the duodenum. The site of election for division of the ring is anterior, near the origin of its duct.

Partial resection of the ring has been employed in two cases with complete recovery in one instance and the probable persistence of symptoms in the other (Cases 3 and 10). Simple division of the ring has been followed by complete recovery in one case, complicated by the occurrence of an intra-abdominal abscess requiring drainage, which, in turn, was followed by a pancreatic fistula of alarming severity (Case 5). In one case, division of the ring was combined with a Hemeke-Mikulicz plastic on the constricted duodenum, necessitated by failure of the constriction to unfold following release (Case 7). In this case a small pancreatic fistula closed spontaneously and complete recovery followed.

In general, direct attacks on the site of constriction are more appealing than indirect attempts to by-pass the obstruction. The recognized failure of gastro-enterostomy to cure cases of chronic duodenal ileus when the obstruction is at the ligament of Treitz would lead to the prediction that failure to relieve symptoms might follow the employment of this operation in annular pancreas. The evaluation of the optimum method demands a critical review of the mortality, as well as the complications and results. Four deaths occurred in the series, three following gastro-enterostomy and one as the result of an advanced acute hemorrhagic pancreatitis in which no

attempt was made to relieve obstruction. This high mortality is not interpreted as condemning the traditionally safe operation of gastro-enterostomy. More significant perhaps is the absence of mortality in four cases of direct attack on the ring, which is a simple, easily performed procedure, offering no particular hazards aside from possible pancreatic complications. The danger of pancreatic fistula, however, is real, it occurred in two instances out of four. Howard's⁵ experience with this complication, notwithstanding the ultimate recovery of his patient, led him to advise duodenojejunostomy in place of direct attack, and Zech,⁷ also the victim of fistula, offered the same advice. Truelsen⁹ fears not only fistula but also pancreatic necrosis and, therefore, advises either gastro-enterostomy or duodenojejunostomy. As already stated, the latter operation has never been tested in this condition. It may be pointed out, however, that the anatomic relationships following this operation, particularly in relation to gravity drainage, would be quite different when performed in the first portion of the duodenum than when performed, classically, in the third portion. Furthermore, damage to the common bile duct is a danger of duodenojejunostomy at this level.

Although pancreatic fistula may occur following division or resection of the ring, attention to the anatomy of the annular duct suggests the possibility of minimizing the chance of its occurrence. It will be remembered that the duct originates with great constancy near the head of the pancreas anteriorly (Fig 5). It is obvious, therefore, that the site of election for division is anterior, as near to the head of the pancreas as the safety of the pancreaticoduodenal vessels will permit, at this level the duct may be entirely avoided and, at the worst, will be cut across as a small twig at its origin. The danger of a postoperative pancreatic fistula should thereby be less than if the ring were divided further to the right, distal to any considerable bulk of secreting pancreatic tissue. Careful closure of the cut surface of the ring with interrupted fine silk sutures, according to the modern practice in pancreatic resection, is an added safeguard.

To summarize the available therapeutic data, there has been only one cure following gastro-enterostomy alone, in a case in which the obstruction was not primarily due to annular pancreas, and one cure following gastro-enterostomy combined with duodenorrhaphy. Of four direct attacks on the ring, three were followed by complete cure and one by indefinite persistent symptoms. The score is apparently slightly in favor of the division of the ring but the figures are too meager to warrant a positive opinion. One can at least state, on the credit side, that attack on the ring seems logical and that it has not resulted fatally and has effected more cures than failures. On the debit side, the danger of fistula is present.

There seems to be justification, therefore, for tentatively advocating the following operative procedures: (1) Exposure of the annula and careful dissection to separate it from the duodenum. (2) Division of the ring as far to the left anteriorly as possible. (3) Resection of a sufficient portion of the ring toward the right and posteriorly to ensure adequate release of the duodenum. (4) If there is not complete expansion of the constricted

bowel, longitudinal incision of the structure with transverse closure after the method of Zech⁷ (5) Ligation of presenting ducts in the cut surfaces of the pancreatic ring, followed by careful closure with interrupted sutures of fine silk (6) Closure of the abdomen without drainage

CONCLUSIONS

Annular pancreas is in some instances a disease of definite clinical significance, demanding surgical treatment when symptoms are present. The results of such treatment to date are encouraging. The reports of additional surgically treated cases are urgently needed in order to evaluate the proper therapeutic approach.

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EFFECT OF REMOVAL OF MALIGNANT THYMIC TUMOR IN A CASE OF MYASTHENIA GRAVIS[†]

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THE FREQUENT ASSOCIATION of thymic abnormalities with myasthenia gravis has been noted by an increasing number of observers, and detailed information concerning this relationship has been given recently by Blalock, Mason, Morgan, and Riven,¹ Miller,² Aronson,³ and others. Tabulation of all lesions of the thymus found in patients with myasthenia gravis was begun in 1917 by Bell,⁴ who collected 56 cases of myasthenia gravis between 1901-1917, in which autopsies or operations had been performed, and in 27 of these thymic lesions were found. In 1935, Norris⁵ reported the autopsy findings

TABLE I

Case No	Year	Author	Patient		Thymus	
			Age	Sex	Enlarged or Persistent	Tumor
		Symmers ⁶				7x5x3 cm
55	1932	(Case 23)	56	Male		Perithelioma
56	1936	Meister ⁷	34	Male		Lympho epithelioma with metastases to pleura
57	1939	Leriche & Jung ⁸				Tumor
58	1940	Miller ²	35	Male	7x3x1.5 cm each lobe 60 Gm	
59	1940	Miller ²	45	Male	6x6x1 cm 30 Gm	
60	1940	Miller ²	27	Female		2x1.5x1 cm Encapsulated
61	1940	Miller	34	Male		5x3x6 cm 70 Gm Encapsulated
62	1941	Campbell ⁹				Tumor—Operation—Death
63	1941	Campbell ⁹				Tumor—Operation—Improvement
64	1941	Aronson ³				5.3x3x1.8 cm 16.6 Gm
65	1941	Blalock <i>et al</i> ¹⁰	33	Male	λ	
66	1941	Blalock <i>et al</i> ¹⁰	28	Female	λ	
67	1941	Blalock <i>et al</i> ¹⁰	22	Female	Rt 9x2.5x0.8 cm L 1.5x2.5x0.8 cm	
68	1941	Blalock <i>et al</i> ¹⁰	39	Female	Rt 9x3x0.8 cm L 1.5x2x0.5 cm	
69	1941	Blalock <i>et al</i> ¹⁰	30	Female	Rt 8x2.5x0.8 cm L 8x2.5x0.8 cm	L U pole 9x1x0.8 cm
70	1941	Blalock <i>et al</i> ¹⁰	34	Female	12x2.5x8 cm	
71	1939	Duvour <i>et al</i> ¹¹	37	Female		6x1x2.5 cm 35 Gm Lymphocytoma—benign

Mention should be made of three cases cited by Meister⁷ in two of which the diagnosis of myasthenia gravis was in question and in the third, the origin of the tumor was doubtful.

(1) Matras and Priesel. White male age 56 had ptosis of both eyelids and disturbance of speech. At autopsy a benign lympho epithelioma of the thymus was discovered.

(2) Matras and Priesel. White male age 35 died following operation for removal of mediastinal tumor which proved to be an epithelioma of the thymus. Six months before this the patient suffered with extremely rapid fatigability but myasthenia gravis was not considered.

(3) Mann L. White female age 41 with history of myasthenia gravis for several years. At autopsy a tumor was found in the posterior mediastinum which was considered to be thymic in origin by two other investigators (Gold and Meister).

in four cases of myasthenia gravis, in two of which thymic tumors were found. He collected five additional cases, bringing the total to 35 instances of thymic

* Read before The Southern Surgical Association, Pinehurst, N C, December 9-11,

lesions found in 80 autopsies and operations in myasthenia gravis. This tabulation was continued by Blalock, Mason, Morgan, and Riven,¹ in 1939, who added 18 cases of myasthenia gravis with thymic lesions proven by autopsy or operation, and to this list we have added 17 cases, including the series of six cases reported in 1941 by Blalock, Harvey, Ford, and Lilienthal¹⁰ (Table I). Thus, in a total of 129 autopsies and operations performed in cases of myasthenia gravis, thymic lesions in the form of persistence, enlargements, or tumors have been found in 71 instances, or 55.04 per cent. Such consistent findings in over 50 per cent of myasthenics would indicate, without question, some intimate connection between such thymic lesions and the disease process itself.

During the past five years the number of proven instances of the association of thymic pathology with myasthenia gravis has doubled, indicating the significance of Norris's⁵ statement that "pathologic changes may be found in cases of myasthenia gravis in direct ratio to the care with which they are sought." This presents the possibility of abnormal changes in thymic function being present in all cases of myasthenia gravis, and adds to the necessity of close investigation of such function in every patient with this disease.

To date, remarkably few attempts have been made to influence the course of myasthenia gravis by surgical methods, and these have been described by Blalock, Harvey, Ford, and Lilienthal¹⁰. Including a personal case, they recorded the details of eight operations performed upon myasthenics, five of which were done for removal of enlarged or persistent thymus. With the exception of Blalock's case, the results of these operations could hardly be called encouraging, since there were three postoperative deaths, and little or no evidence of improvement of the myasthenic status in the other five. The operative procedure used in the nontumor group might be criticized on the basis of incompleteness, since only neck incisions were made and the anterior mediastinum probably was not adequately exposed. Blalock's case represents the first and only report of a cure of myasthenia gravis, and this was accomplished by the removal of a benign thymic tumor in a patient rapidly declining with the disease who had had all of the various medical measures employed as well as roentgenotherapy. The marked clinical improvement of this patient has been nothing short of spectacular, since she has remained free from all evidences of the disease for five and one-half years. So far as can be determined, a remission of this duration has not been produced by medicinal or roentgenotherapy in a patient in whom the disease had reached such a severe state.

During the past summer, Blalock, Harvey, Ford, and Lilienthal¹⁰ have advanced the possibility of the potential benefits from surgical intervention in cases of myasthenia gravis by performing thymectomies upon a series of six patients in various stages of the disease. Postulating the similarity of the symptoms of myasthenia gravis with the effects of curare poisoning, they suggested that some particular tissues of the body might produce a similar substance. Since the thymus is the site of pathologic changes in such a large

percentage of myasthenics, they reasoned that such an abnormal secretion might originate there, and therefore, suggested exploration of the thymic region. Perhaps insufficient time has elapsed since these operations were performed to evaluate the results without bias, but the definite and striking "improvement that has taken place in most of the patients indicates that the thymus is concerned directly in the pathogenesis of the disease"¹⁰

The type of lesion found in the thymus in the 71 autopsies and operations was noted to be an enlargement or persistence in 30 instances, and a definite tumor was found in 41 instances. Microscopically, the thymic remnants presented a picture typical of simple hyperplasia and this term has been used in many descriptions. The tumors of the thymus present a more difficult problem of classification because of uncertainty regarding the origin of certain cell elements of the thymus. Also, confusion has arisen over what tumors found in the mediastinum might properly be termed true thymic neoplasms, but most authorities agree that this can be determined on a basis of (a) location, (b) shape, (c) morphology, and, according to Foot,¹² (d) failure to invade bone, (e) tendency to spread by extension to the surrounding pleura and pericardium, and (f) failure to metastasize below the diaphragm. Of the 41 instances of thymic tumors found at autopsy or operation, 37 were described as benign thymomata, and four were classified as malignant tumors. The four malignant tumors were discovered at autopsy.

Case Report—J B G W, white, male, age 52, was seen in consultation, July 30, 1941, with Dr H Ansley Seaman, of Waycross, Ga, in regard to the treatment of a tumor in the anterior mediastinum associated with myasthenia gravis. The first symptoms of myasthenia gravis appeared in September, 1939, with development of marked drooping of the left eyelid and weakness of the muscles on the left side of the face. He also noted slight weakness in swallowing and talking, and consulted a rhinolaryngologist who found no definite cause. These symptoms persisted for six weeks. In December, 1939, he suffered an attack of acute appendicitis which was treated by operation and followed by uneventful convalescence.

The next exacerbation occurred one year later and lasted about one month. His jaws and tongue became so tired that he could scarcely talk. In January, 1941, without fully recovering from the former attack, the patient became acutely ill with an upper respiratory infection (influenza) which lasted for ten days. Following this, all symptoms of myasthenia gravis became rapidly and progressively worse. Within a month he noted general weakness especially marked in the late afternoon and evening, and weakness of the tongue and throat muscles became so severe that the patient was able to talk for only a few minutes at a time. Weakness of jaw muscles prevented proper mastication of food and the patient lived on a liquid and soft diet.

March 28, 1941, he was seen by Dr J G Lyeily, Jacksonville, Florida, who confirmed the diagnosis of myasthenia gravis and prescribed prostigmine, 15 mg, t i d. This was followed by definite improvement, which was described by the patient as "giving more strength to talk and swallow." He felt that he could not get along without the drug and discontinued it only after it caused severe gastric reaction (nausea, vomiting, and pain). Prostigmine was then discontinued and ephedrine substituted. This produced equally beneficial results and was not followed by troublesome side-effects.

Early in May, 1941, he was examined by Dr William B Porter, of Richmond, and Dr Edwin Lehman, of Charlottesville, Virginia, while they were conducting postgraduate clinics in Waycross. In addition to the weakness of jaw and face muscles, they noted

the absence of the pharyngeal reflex and the diagnosis of myasthenia gravis was again confirmed. They suggested the possible association of a thymic tumor, and roentgenograms of the chest were made which revealed the presence of a sharply circumscribed, moderately dense shadow in the anterior mediastinum on the level with the third, fourth, and fifth costal cartilages (Figs 1 and 2)

In June, 1941, the difficulty in swallowing became so severe that he was sent to the hospital for nasal feedings for a period of ten days. At this time food regurgitated into his nose, and mucus was so profuse that continuous suction was instituted to prevent choking. Examination of the spinal fluid was negative, and no sugar was found in the



FIG 1—Roentgenogram, July 31, 1941, showing circumscribed shadow in anterior mediastinum



FIG 2—Lateral view showing same shadow in anterior mediastinum

urine. Blood count essentially normal. Blood pressure 138/80. There was no evidence of muscle atrophy or degeneration, and no changes in reflexes except the pharyngeal. No roentgenotherapy was given.

At the time of this examination, July 30, 1941, it was obvious that the disease was progressing rapidly, as evidenced by marked general weakness, which kept the patient in bed most of the time. Talking and swallowing were accomplished with extreme difficulty, since all symptoms were worse in the throat region. The question of removal of the tumor was discussed with the patient, who quickly made the decision since he felt that his condition "was hopeless unless something could be done."

Operation—August 16, 1941, Ware County Hospital, Waycross, Ga. (Doctors Poer and Seaman). Anesthesia by local and block infiltration of novocain hydrochloride, 1 per cent. (Sodium pentothal, 25 per cent, given intravenously for last 20 minutes of operation—Dr. B. R. Bussell). A slightly curved incision was made from the second to seventh rib level along the right margin of the sternum and carried through the soft tissues to the surface of the cartilages. The periosteum of the third, fourth, and fifth costal cartilages was divided for a distance of approximately 5 to 7 cm and 4 cm of each of these cartilages was removed. The right border of the sternum was removed with rongeurs for a distance of 1 cm. A greyish-yellow tumor, located in the thymic region of the anterior mediastinum, immediately came into view and could easily be separated from the sternum by blunt dissection with the index finger. The tumor was freed from the surrounding structures and found to lie on the pleura, pericardium, and large blood vessels. A small opening was accidentally made into the right pleural cavity which caused respiratory embarrassment for a few moments until closed with silk sutures.

The tumor was very soft and broke apart on removal, but was so well encapsulated that every portion could be identified and removed. The wound was closed in layers using interrupted sutures of black silk. Convalescence was complicated by two "sinking spells" accompanied by extreme cyanosis. Oxygen and prostigmine successfully relieved these symptoms.

Subsequent Course—Before the patient left the hospital he was given two light roentgen ray treatments over the anterior mediastinum, but each of these was followed by evidence of shock and, therefore, they were discontinued. He was again given prostigmine for one week after operation and has taken ephedrine at irregular intervals.



FIG 3—Photograph of the patient, December 5 1941, showing scar of operation



FIG 4—Photograph of gross specimen

since. In November he developed acute pyelitis which confined him to bed for two weeks. He is now working regularly as a salesman, drives his own car, has no difficulty in swallowing, and can talk indefinitely without fatigue (Fig 3).

Pathologic Examination—*Gross* Dr. Warren B. Matthews: "The specimen consists of a tumor, and parts of three surgically resected ribs. The rib pieces are each between 3 and 4 cm. in length and include the costochondral junction. These rib segments are grossly normal (Fig 4).

"The tumor is a thin, fibrous shell filled with a putty-like greyish-yellow, crumbly material. It weighs 47.5 Gm. after formalin fixation, and measures externally 6.5 x 4.9 x 2.5 cm. The putty-like content is easily removed from the capsule, leaving a partly loculated interior. The fibrous capsule dips in, forming shelves that project into the cavity of the tumor. Nowhere is the material inside the capsule intimately adherent to the capsule. The tumor is uniform throughout in appearance. In places the capsule is so thin that it is almost translucent. The exterior of the mass is rough, and covered with stringy connective tissue fibers and bits of fat.

Microscopic Capsule: Three sections taken from the capsule of the tumor show that this is made of fibrous tissue with various degenerative changes. In places there are small granular amorphous calcifications. Zones of cholesterol and other lipid deposits, with crystal clefts, are noted. These vary considerably in size. The connective

tissue is old and relatively avascular, containing relatively few nuclei. In the loose areolar tissue on the outside of the mass there are a number of small collections of lymphoid tissue. Some of these have a definitely follicular form. In only one place in these three capsule sections is the tumor adherent to the capsule.

"Tumor. All sections reveal a tumor made up of fairly large pale cells, apparently epidermoid, arranged in massive sheets (Fig 5). Cellular outlines are poorly differentiated. In places the cells seem to assume no particular arrangement, in other places, the tumor cells are peritheliomatous, extending radially from the numerous thin-walled blood vessels present (Fig 6). The nuclei are large and ovoid. They contain little



FIG 5—Photomicrograph showing general characteristics of the tumor made up of large pale cells, apparently epidermoid, arranged in massive sheets. Numerous fat filled macrophages are noted. (X100)

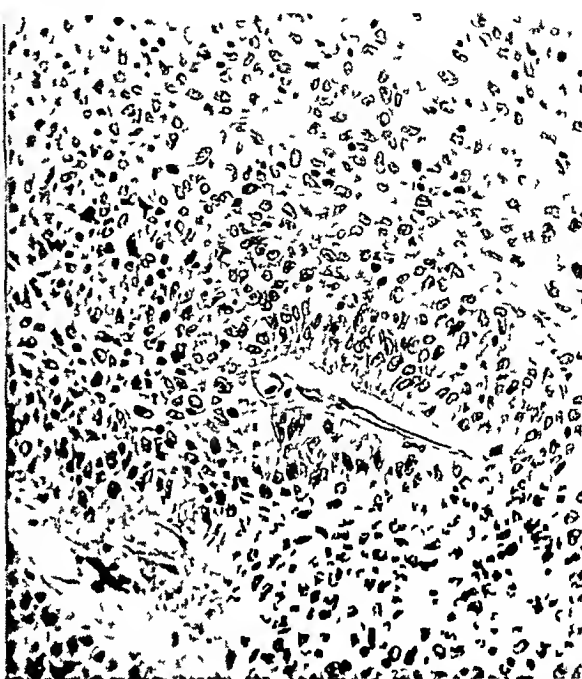


FIG 6—Photomicrograph of a section through a mass of tumor cells illustrating the perithelial arrangement noted in many places. (X200)

chromatin, and in most cases a single large nucleolus. There is some anaplasia although few mitoses are noted. From place to place, isolated amorphous deposits of material resembling keratin are noted. These are concentric and may be abortive Hassall's corpuscles. The fibrous stroma is scarce. Scattered throughout the tumor are a few lymphocytes and a few lipid-filled endothelial leukocytes. *Pathologic Diagnosis* Low grade carcinoma, probably thymic in origin."

DIAGNOSES OF CONSULTANT PATHOLOGISTS

Dr Everett L. Bishop (Atlanta). Slide shows massive keratinization and lamellation with much cholesterol and lipid structure. Calcification is present. Flattened cells show not many mitoses. There are occasional small cysts lined by cuboidal epithelium and various sized masses of hyaloid material. This is a dermoid or teratoid tumor of low malignancy (carcinoma) without definitely designating the point of origin, although some parts suggest thymus.

Dr Sam Blackman (Johns Hopkins Hospital). The tumor is made up of sheets of epithelial-like cells which contain a considerable amount of pale cytoplasm and large ovoid nuclei with little chromatin and a single large nucleolus. The cells have a definite and characteristic lobular arrangement and in places they seem to extend radially from the numerous thin-walled endothelial lined vascular channels. Scattered among the epithelial cells there are lymphocytes. Few concentric masses of hyalinized material are

found which appear to arise from the epithelial cells of the tumor and closely resemble Hassall's corpuscles. The tumor cells show some anaplasia but mitoses are not frequent. The picture is typical of the so-called carcinomata of the thymus and is relatively benign but tends to metastasize in the late stages.

Dr N Chandler Foot (New York Hospital). The tumor is composed of thymic reticulum cells which are ectodermal and quasi-epithelial and not related to the ordinary reticulo-endothelium. It has a definitely perithelial arrangement of cells, sometimes rather strikingly epithelial in appearance. Abortive Hassall's bodies are to be found here and there. The tumor is definitely malignant of a type described by Symmers (perithelioma).

Dr Douglas Symmers (Bellevue Hospital). There are numerous blood vessels in the growth and tumor cells are arranged around their long axes for a row or two, after which the growth of the cells becomes disorderly. I have not been able to trace any connection between the vascular wall and the origin of the tumor cells. However, the vascular wall is extremely thin in the great majority of instances and represents merely an endothelial-lined slit. The tumor is malignant—and probably highly malignant. If one insists upon giving it a name, I think that "perithelioma" or "perithelial sarcoma" would suffice.

Dr Murray Copeland (Baltimore). The sections show marked hyperplasia and multiplicity of Hassall's corpuscles with only a moderate amount of lymphoid stroma. Consensus of opinion is that it is an unusual type of low-grade carcinoma of the thymus.

Discussion—The difficulty of writing down a generally acceptable classification of thymic tumors has been mentioned. Ewing's^{1,3} statement has been quoted frequently, to wit: "No group of tumors has more successfully resisted attempts at interpretation and classification than those of the thymus. The problems involved include those which have complicated the embryologic and histologic study of the gland, while added difficulties arise from the comparative rarity and considerable diversity of the tumors, and from the somewhat imperfect knowledge of the general pathology of the thymus." He classifies thymic tumors as carcinoma, lymphosarcoma, and granuloma (Hodgkin's disease). Symmers⁶ has studied a fairly large group of autopsy specimens from cases with thymic and thymic-like growths and found two associated with myasthenia gravis. While objecting vigorously to the use of the term "thymoma," he suggests the classification: (1) perithelioma, (2) epithelioma, (3) lymphosarcoma, (4) spindle cell sarcoma, and (5) Hodgkin's granuloma.

Along with the difficulties that have arisen in the proper classification of thymic tumors, some confusion has been found to exist in regard to the cellular activity of such tumors, making the clear distinction of malignancy somewhat questionable in some cases. Bell⁴ mentions this possibility in criticism of the case reported by Meggendorfer in 1908, when he stated that insufficient information was given in his microscopic description of the tumor. Two other instances of malignancy of the thymus associated with myasthenia gravis are the autopsy cases reported by Symmers⁶ in 1932. He classified these as perithelioma and lymphosarcoma.

Meister,⁷ in 1936, described the autopsy findings in a case of myasthenia gravis in which a nodular tumor was discovered in the anterior mediastinum, with metastases to the right parietal pleura. Two types of cells were found on microscopic examination, those resembling lymphocytes and others of

typical epithelial appearance which had undergone malignant change. In classifying this tumor as a lympho-epithelioma, he states his belief that many thymic tumors reported as carcinoma or sarcoma were in reality of this same type.

No record of an operation for the removal of a malignant thymic tumor has been found, and all information regarding tumors of this type has been gathered from autopsy reports.

CONCLUSION

The association of thymic lesions with cases of myasthenia gravis has been reviewed and 71 proven instances have been collected from the literature. During the past five years, over two-thirds of the cases of myasthenia gravis, in which the thymus was examined at autopsy or operation, were found to have definite pathologic changes in the thymus. This fact, plus the results obtained by removal of one thymic tumor and six thymic enlargements by Blalock, Harvey, Ford, and Lilienthal,¹⁰ indicates that the thymus, definitely, is concerned with the etiology of myasthenia gravis.

The removal of a malignant tumor of the thymus in a case of myasthenia gravis is recorded. This, apparently, is the only case of this type that has been recorded during the life of the patient. The marked clinical improvement that has resulted adds to the growing evidence that the thymus is partly if not entirely responsible for the disease. This experience, plus that of Blalock and his collaborators, would indicate that every patient suffering with myasthenia gravis should be offered the possible benefits of removal of the thymus regardless of the presence of a definite tumor.

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DISCUSSION —DR. JOSEPH E. J. KING (New York, N. Y.) I am not capable of discussing Doctor Poer's paper but I wish to say that, at the last meeting of the New York State Medical Society, Doctor Campbell, of Albany,

reported a somewhat similar case, with successful removal of the tumor, and I shall be glad to send this report to Doctor Poer

DR E D CHURCHILL (Boston, Mass) I have enjoyed this presentation greatly It is a very important case to place on record I am not so certain, as yet, what general conclusions can be drawn from it, because thymic surgery is still in a formative state

I have had three patients in the last ten years in whom I, as a surgeon, made a clinical diagnosis of myasthenia gravis All three had thymic tumors, shown roentgenographically They were recommended to the hospital and studied by the neurologists, who know more than I do about myasthenia gravis I was told that these patients did not have myasthenia gravis, much to my disappointment Then I found that the neurologists have an exact, but empirical, definition of myasthenia gravis It is a disease entity based on the response to injections of prostigmine The patients I refer to did not meet this specific definition Possibly they would have been labeled myasthenia gravis before the definition of the disease by the prostigmine test had been established

What I am driving at is this Myasthenia gravis is a syndrome without established etiology and without a universally recognized and accepted pathologic finding in the thymus On the basis of the prostigmine reaction, a great majority of patients with this syndrome are now labeled true myasthenia gravis, a few of these have thymic tumors Certain other patients with thymic tumors and similar symptoms, but not reacting to prostigmine, are not properly termed myasthenia gravis The best recorded responses to thymus ablation—as in the case here recorded—are in those patients with demonstrable thymic tumors To conclude that the thymus should be removed in cases of myasthenia gravis without tumor is a jump ahead of the evidence In carefully selected cases, however, this operation may be justified for the compilation of further data

DR BARNEY BROOKS (Nashville, Tenn) The patient reported from my clinic by Doctor Blalock, who showed such marked improvement of myasthenia gravis following the extirpation of a mediastinal tumor, showed a remarkable response to prostigmine over a long period prior to operation, and I do not believe I have ever seen a more dramatic effect of the drug than occurred in the use of prostigmine in Doctor Blalock's patient At times the muscle exhaustion would become so great that artificial respiration would have to be resorted to, to keep the patient alive until the injection of prostigmine could be administered Immediately after the injection, not only was the patient's respiration restored, but normal strength seemed to be immediately restored to all muscles of the body

DR D HENRY POER (Atlanta, Ga, closing) In reply to Doctor King, and in regard to Eldridge Campbell's two cases, they were included in Blalock's recent article and, therefore, have been tabulated in Table I One of these patients died suddenly two days after operation, and the second is improved, but there has been persistence of the myasthenia gravis

Doctor Churchill brought out some pertinent points regarding the association of myasthenia gravis and thymic tumors The first of these concerns an accurate diagnosis of myasthenia gravis, in this group several diagnoses have been made on very meager evidence, such as weakness of one group of muscles and abnormal fatigability Perhaps a syndrome of some of these same symptoms may also be associated with mediastinal tumors as suggested by Doctor Churchill The diagnostic tests of Viets in which the reaction to prostigmine is measured, plus the quantitative studies of the state of neuromuscular con-

duction described by Harvey and Masland (cited by Blalock) have made it possible to establish the diagnosis of myasthenia gravis. In the case of the patient reported here, the diagnosis was made by a neurologist who observed the beneficial response to prostigmine.

The cases operated upon by Doctor Blalock during the past summer, in which the thymic remnants were removed, will be followed with much interest. Since remissions of varying duration are known to occur in this disease, we will have to wait some time before attempting to evaluate the end-results. My thought in presenting our case was to make us more conscious of the thymus in patients with this disease in the hope that more conclusive evidence of their relationship may be obtained.

SUCCESSFUL EXPERIMENTAL LIGATION AND DIVISION OF THE THORACIC AORTA*

JAMES C OWINGS, M D , AND JOHN F HEWITT, M D

BALTIMORE, MD

FROM THE DEPARTMENT OF SURGERY OF THE JOHN'S HOPKINS SCHOOL OF MEDICINE, BALTIMORE, MD

WE WISH TO REPORT a new method that we have used for successful ligation and division of the thoracic aorta. Doctor Halsted¹ nearly succeeded in occluding the vessel by external pressure, and both Doctor Reid² and Doctor Pearse³ succeeded in blocking it by inserting foreign bodies into the lumen. Doctor Peaie⁴ also reported successful occlusion after external application of a band of cellophane in 1940. It was of great interest to us that Doctor Halsted had been able to constrict completely any of the large blood vessels except the thoracic aorta. After careful reading of his very complete papers, it seemed to us that there were probably two reasons for his failure. First, the change in the caliber of the vessel had always been made very abrupt and, second, that it had usually been produced by a very unyielding substance, namely, an aluminum band. We, therefore, outlined a series of experiments in which the constriction was to be made in the form of an hourglass, using for the purpose materials that would give to a certain extent with the pulsation of the vessel. We later changed the form of the constriction to the shape of a funnel with the large end pointing toward the heart. In the early experiments preserved fascia lata was used, but Doctor Hewitt and I found, as other people had previously reported (Reid² and Pearse⁴), that this substance soon disintegrated and allowed the vessel to widen its lumen. We next tried a double layer of the best quality silk cloth, but this was not satisfactory because it tended to wrinkle up like an accordion and also caused too much local tissue reaction. In time, the vessel opened under the cloth, allowing pressure to be reestablished in the aorta below the band before collateral circulation had been established. In order to prevent this from happening, we conceived the idea of applying a section of ordinary stationer's rubber band over the silk band, as a second stage. Finally, after about two years' work with only one successful experiment, we abandoned all other materials in favor of rubber. It seemed best for several reasons. It could be easily molded to the desired shape by mattress sutures, it gave well with the pulsation of the vessel, and caused very little tissue reaction by comparison with the other materials. We soon found that it was necessary, no matter what the material used, to produce the constriction always in two and usually in three stages in order to keep the pressure above the bands high enough to produce sufficient collateral circulation. At first we waited six weeks to two months between operations, but found that this was too long because the vessel opened too widely. We then tried a series where a lapse of only two weeks was allowed, but found that

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941.

this was too short a period because, although the pressure below the bands had not been reestablished, neither had the collateral circulation been sufficiently developed. We lost six animals from what we considered to be too tight an application of the second or third band, and six more when we tied and divided the vessel. We came to the final conclusion that three weeks was about the right interval between the first and second stages and that three to six weeks between the time of application of the second and third bands was most likely to be successful.

Our final technic is as follows. The animal, a dog, is given 0.25 gr. of morphia and anesthetized with ether supplied through an intratracheal tube with air pressure. The left side of the chest from about the middle of the scapula to the twelfth rib is shaved and cleaned up with two coats of 3.5 per cent iodine, which is removed in turn by the application of 70 per cent alcohol. The chest is opened in the midaxillary line of the fourth interspace. The ribs are retracted by a self-retaining retractor and the lung is held aside with a spatula. This gives good exposure to the descending portion of the arch and the upper portion of the thoracic aorta. The vessel is freed from the posterior chest wall by blunt dissection with a small curved clamp. Next, a strip of the best sheet rubber 1 Mm. thick and 1 cm. wide is drawn around the aorta just above the first intercostal artery. It is tightened in the shape of a rather wide-mouthed funnel by means of mattress sutures of silk. The first suture is placed so as to decrease the caliber of the vessel very little. Each successive one, however, is placed so as to make the band tighter, and the final one so that only a very faint thrill is felt below the band and the vessel wall seems flabby. The silk sutures are tied down tight in order to try to bury them in the rubber so that they will not come into direct contact with the vessel wall. The width of the band can be varied according to the size of the vessel. The rubber is boiled with the instruments for the same length of time. Two sutures of braided silk are used to appose the ribs, after the air has been expressed from the pleural cavity, by fully expanding the lungs with positive pressure through the intratracheal tube. The chest wall is then closed in layers with black silk. Three weeks later the chest is opened through the fifth interspace. If the pressure is found to have returned to the section of the aorta below the band, a second rubber band is applied in the same manner between the first and second intercostal arteries and tightened to the same degree as the first one and closure made in the same manner. If, however, pressure is found to be still very low, nothing is done at this time.

If a third stage is found to be necessary, about a month or six weeks is allowed to elapse depending upon how high the tension was found to be at the second stage, and a third band is placed one intercostal artery lower in the same manner as the first two.

A month or six weeks is again allowed to elapse before the chest is reopened, at which time the vessel is ligated just below the last band and again about 1 cm. distal to it, the ligatures being of doubled C silk. The section of the vessel between the ties is crushed with a Kelly clamp to promote fibrosis.

for Schlemmer

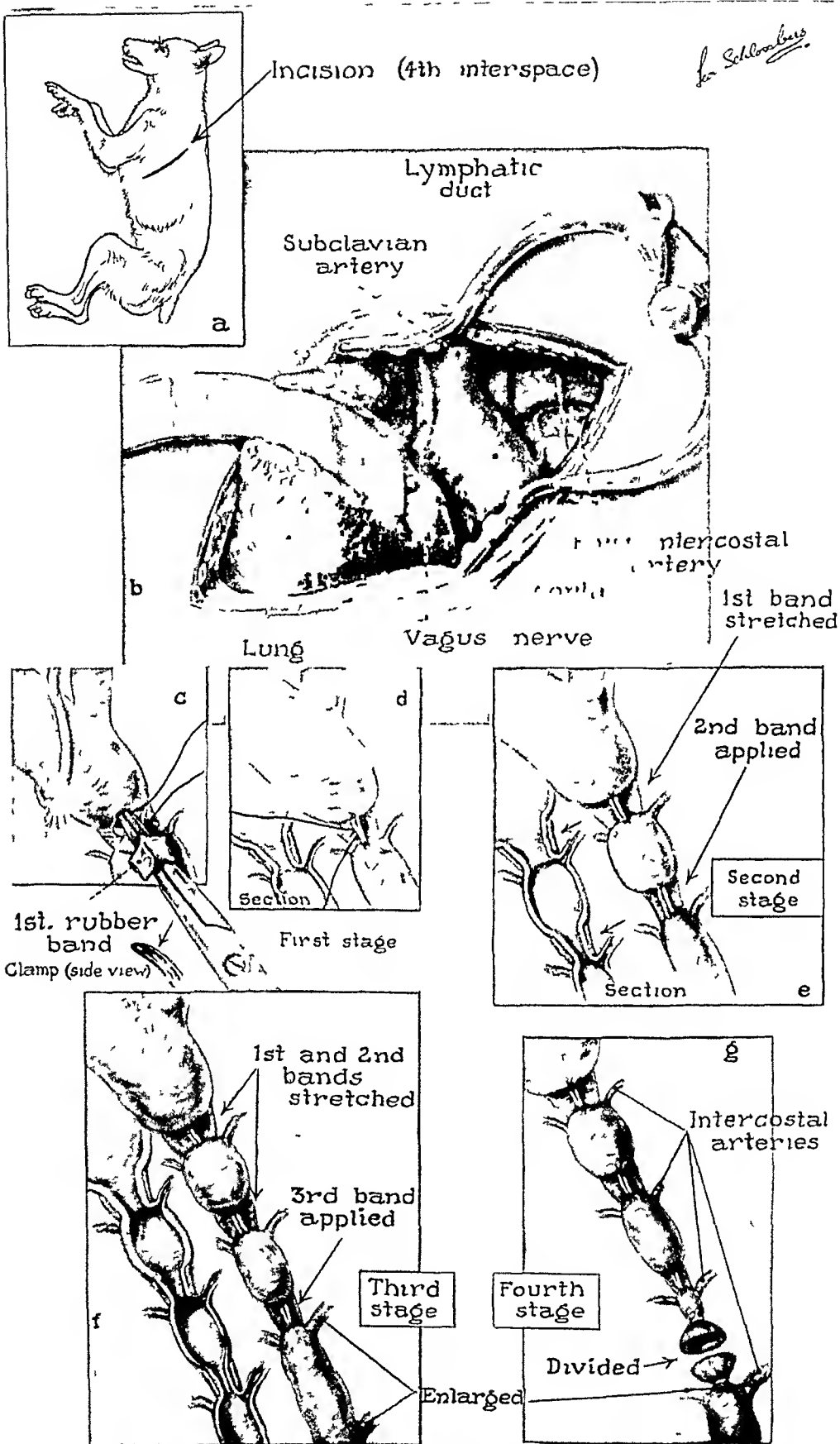


PLATE I—Demonstrates technic of applying rubber bands. They are made of the best sheet rubber, 1 mm thick and about 1 cm wide, and tightened in the shape of a funnel by mattress sutures of silk. The ligation and division are shown as a single stage but in reality were usually done as separate steps. The intercostal vessels become greatly dilated below the most distal point of constriction.

Finally, time enough has to be allowed for the crushed segment to become fixed before dividing it, or else the cut ends have to be tied together to prevent retraction. Every time we attempted ligation and division in one step without tying the ends together the animals died, even though they could stand up and wag their tails immediately after they came out from under anesthesia. We feel that this was due to the fact that the ends of the aorta usually retracted well over an inch, which in turn probably caused angulation of the intercostal vessels. This angulation apparently disturbed the collateral circulation to such an extent that it became insufficient. We found this out by reviewing the notes on the first successful animal in which there had been considerable bleeding at the time the aorta was divided. This forced us to transfix the intercostals near the field of operation with sutures of silk which prevented the ends of the aorta from retracting. Plate I demonstrates in detail the various steps of the operative procedures.

The results of the whole group of experiments may be summarized as follows. During the course of the work, 75 dogs and four cats were used, and the chest was opened 162 times. Seventeen of the animals died from distemper, seven from empyema, 12 from what we consider to be insufficient collateral circulation, six from having the band drawn too tight, one from anesthesia, two from accidental death in a dog fight, four were sacrificed, and 28 died from hemorrhage due to the various types of bands cutting through the wall of the aorta. It can be readily seen that by far the commonest cause of death was hemorrhage. The first band cut through 14 times, the second band ten times, and the third band twice, and two animals died from secondary hemorrhage due to inadequate control of bleeding from collateral vessels. Only six animals of the whole series lived any appreciable time, and two of these had to be killed because of paralysis in the hind extremities, one after two and one-half months, and the other after six weeks. The remaining four would probably have lived indefinitely and, therefore, must be considered as successful experiments. The protocols for these four animals are presented in detail.

PROTOCOLS OF FOUR SUCCESSFUL EXPERIMENTS

Dog No 16—October 27, 1937. Grayish black female, fairly large, solid color, given 0.25 gr morphine hypodermically and anesthetized with intratracheal ether. Chest opened in fourth interspace and aorta, which was considerably larger than average, constricted in the usual manner by a band of doubled glove silk. When we had finished, the band did not feel tight enough, so it was further tightened by a tie of braided silk until a bare thrill could be felt. Constriction was made just below the arch and above the first intercostal. The dog stood the operation well.

November 24, 1937. Chest reopened, aorta below the tie was found to be still flabby and a thrill could be felt. Much more blood was going through than when the first constriction was made. Aorta again compressed by two ties of braided silk, one over the lower end of the silk band and one about 2 cm below this, which were tied down until a bare thrill could be felt.

January 31, 1938. Aorta had returned to about the size it was on November 24. It was again constricted, this time by a rubber band placed between the two braided silk ties and tightened until the vessel wall was flabby and only a faint thrill could be felt.

March 16, 1938. Aorta still flabby and only a bare thrill was felt but tension did seem a little higher than when noted on January 31. The heart seemed greatly dilated. Chest closed without doing anything to the aorta.

June 8, 1938. Aorta completely tied off with doubled braided silk just below the lowest point of constriction. Before the tie was made a faint thrill could be felt but tension in the vessel seemed very low. The animal stood the operation well and had some tone in both hind legs and also in the

tail immediately after operation. The animal did, however, seem to have some respiratory distress and the heart was huge occupying about one fourth of the thoracic cavity.

June 22, 1938. The animal regained the use of the hind legs within 48 hours, and has been active ever since.

May 10, 1939. Animal had been quite healthy during the past year. Chest reopened. The aorta was still rather flabby with no pulsation felt below the ligature, but a very faint thrill was made out so blood was apparently leaking through the site of the tie to some extent. The heart did not seem to be greatly enlarged. The intercostal vessels were quite large and one was perforated during the closure of the chest wall causing bleeding which was controlled only with great difficulty. The aorta was tied twice, once on the normal wall below the old tie and once about 1 cm above this over the old scar tissue of the previous tie. The animal stood the operation well.



FIG 1—Roentgenogram of collateral circulation of Dog No 16 after injection of modified Hill's mass. Aorta can be seen to be interrupted just below the arch and beginning again at about the level of the sixth intercostal. Most of the collateral goes through the internal mammary arteries.

May 15, 1940. Chest reexplored. Fairly good pulse in the aorta but no thrill indicating that there was good collateral circulation but no leak through the point of previous occlusion. The intercostals were very large and a good pulsation was seen in them. Considerable bleeding was encountered in opening the chest wall but was controlled with little difficulty. The aorta was easily exposed, but after being freed a pair of intercostals were found to empty into the segment that was to be cut so these were tied off first. The aorta was then divided between ligatures of doubled C silk. The ends did not retract because the mattress sutures used to tie the intercostals held the two cut ends together. The animal seemed to stand the operation very well.

October 1, 1940. Dog went blind during the summer, and the resident ophthalmologist said that this was due to bilateral retinal separation. She has seemed very well otherwise.

December 16, 1940. Kidney function test: 0.5 cc of phenolphthalein introduced intravenously, 20 per cent in 30 minutes, 30 per cent in 60 minutes, total 50 per cent in one hour.

December 18, 1940. Liver function test: 5 mg bromsulphalein per kilo introduced intravenously. Five minutes, 10 per cent, 30 minutes, 0 per cent.

May 19, 1941. Pressure in right carotid artery 190 mm Hg. Left femoral 137 mm Hg. (Pressures taken by puncturing artery with a small needle connected directly to a mercury manometer.)

July 28, 1941. Blood chemistry: NPN 38, chlorides (as sodium chloride) 468, sugar 68. Kidney function, phenolphthalein 30 minutes, 20 per cent, 60 minutes 25 per cent, total 45 per cent.

DIVISION OF THORACIC AORTA

July 30, 1941 Right carotid was moved up under skin so it could be easily used to determine blood pressure

September 8, 1941 Liver function test 5 minutes, 40 per cent, 30 minutes, 10 per cent Blood chemistry N P N 64, chlorides 514.8, sugar 76

September 10, 1941 Pressure right carotid 182 Mm Hg Right femoral 142 Mm Hg Kidney function test 30 minutes, 50 per cent, 60 minutes, 15 per cent, total 65 per cent

September 29, 1941 Blood chemistry N P N 29, chlorides 495, sugar 80

October 1, 1941 Pressure right carotid 190 Mm Hg Pressure right femoral 140 Mm Hg Liver function test 5 minutes, 30 per cent, 30 minutes, 10 per cent



FIG 2—Shows the blood from the dilated internal mammary arteries continuing through the superior and inferior epigastric vessels back into the iliacs

October 13, 1941 Dog killed today by injecting modified Hill's mass into the left carotid as she was bled from the right jugular vein, in order to demonstrate collateral circulation. Roentgenograms showed that most of the blood was carried by the internal mammary vessels and the phrenic artery into the intercostals below the site of the division back into the aorta and directly through the superior and inferior epigastric vessels into the iliacs. This collateral circulation is well demonstrated in Figures 1 and 2. The tissues looked grossly normal except for the liver, which showed some evidence of chronic passive congestion and the aorta, which showed the changes so well described previously by Doctor Halsted⁵ and Doctor Reid,⁶ that is, a decided thickening of the vessel wall above the point of division, due principally to an increase in the muscle of the media, a replacement of the vessel wall by fibrous tissue under the bands and a tendency of the vessel wall to thin out immediately below the point of division. The eyes were turned over to the Wilmer Institute for study.

November 24, 1941 Microscopic sections of the tissues merely confirmed the gross impression as shown in Figures 3 and 3A.

Dog No. 22—January 29, 1939 Shaggy, long haired white and tan, male. The chest was opened through the fourth interspace. The aorta constricted just above the first intercostal by means of a rubber band until only a bare thrill could be felt and the vessel wall was flabby. The band was very narrow and it was felt that it might cut through.



Fig. 3—Sections (A) and (B) are from Dog No. 30 and (C) and (D) from Dog No. 16. They illustrate the marked thickening that occurred in the media of the aorta above the point of division due to the sustained hypertension in the upper segment



Fig. 3A—(A) is a longitudinal section of the aorta wall of Dog No. 16 taken above the point of division and (B) from below it. They show the same changes in the media as in Fig. 3. There is also complete replacement of the vessel wall by scar tissue where it has been compressed and ligated

April 12, 1939 Chest wall infected, wound opened and silk removed, then loosely closed with catgut sutures

May 15, 1939 Chest reopened through the fifth interspace Since the vessel had opened until there was fair tension below the first band, a second rubber band was placed around the aorta between the first and second intercostals and tightened until only a very slight thrill could be felt

June 28, 1939 Chest explored There was still too much tension in the aorta, so a third band was placed two intercostals below the second one, and tightened to the usual degree

August 21, 1939 Two of the previous wounds were infected and had to be opened so that the silk could be cleaned out and the wound closed with catgut

October 11, 1939 Aorta doubly ligated with heavy braided silk, the first ligature being placed just below the first band and the second about 1 cm below it The portion of the vessel between the two ligatures was crushed with a clamp The dog stood the procedure well and was able to walk as soon as he came out of the anesthesia

October 16, 1939 Dog in good condition Little if any weakness of hind legs

May 13, 1940 Chest reopened Aorta showed very faint pulse below site of ties and no thrill The ties were so near the diaphragm that exposure was difficult A dilated intercostal vessel was torn during the attempt to expose the field of operation and controlled only with considerable difficulty However, the aorta was finally exposed and completely divided under direct vision after having been tied with doubled C silk It did not retract because the mattress suture on the intercostal held the cut ends close together The animal was in good condition postoperatively in spite of considerable loss of blood He was able to wag his tail and stand up

July 7, 1940 The dog had remained in good health, and it had been intended to make physiologic studies on the animal in the fall, but to day he was found dead in the yard of the laboratory, having been killed in a dog fight The tissues were so badly disintegrated that no attempt was made to get microscopic sections Field of operation showed no hemorrhage or infection

Dog No 23—February 6, 1939 Tiny white dog, male The chest was opened through the left fourth interspace, and a band of rubber placed around the descending portion of the aorta just above the first intercostal and drawn down with mattress sutures until the vessel wall below was flabby and only a very slight thrill could be felt

April 17, 1939 Chest reopened, intercostals below previous band were greatly dilated—approximately three times normal No thrill could be felt in the vessel and no pulse below the previous band, but tension seemed normal even when the vessel was completely compressed in the region of the band A second rubber band was applied one intercostal below the first one, almost completely compressing the vessel, but tension still remained high There must have been a large volume of blood entering the aorta below the first band by way of collateral vessels The dog stood the operation well

June 26, 1939 Chest explored Very few adhesions were found No thrill or pulse felt in the aorta below the compressing bands but tension did not seem to be as high as it was on April 17 Vessel doubly ligated one intercostal below point of compression The upper ligature was of braided silk and the lower of doubled C silk The ligatures were placed about 1 cm apart and the wall of the aorta was crushed between them to promote fibrosis The dog stood the operation well and had good tone in the rear extremities as soon as he woke up

May 8, 1940 The dog has been in good health during the past year Chest reopened The intercostals were found to be greatly dilated and much bleeding was encountered in the intercostal muscles No pulse could be felt in the aorta and no thrill below the tie The area between previous points of ligature was found to be collapsed and felt fibrosed Religated with doubled C silk just below previous ties and divided A double ligature was placed on the lower end and a single on the upper end Cut ends were not allowed to retract

May 13, 1940 Dog ate a full meal on night of operation Has no weakness of the legs or tail and has been in fine condition ever since

July 7, 1940 Dog found dead, having been killed in dog fight The tissues were so badly disintegrated that no attempt was made to get specimens for section No physiologic studies had been made Field of operation showed no hemorrhage or evidence of infection

Dog No 30—January 27, 1941 Small shaggy, gray male Left side of chest opened through fourth interspace, and a band of rubber sheeting, 1 cm wide funneled around the aorta between the first and second intercostals and tightened until only a bare thrill could be felt and the vessel wall was flabby

February 17, 1941 Chest reopened The vessel showed a good thrill with fair tension below the band The second band was placed two intercostals below the first and tightened to the usual degree

April 28, 1941 Chest explored Only a very faint thrill was felt in the aorta but pressure below the second band seemed fairly high Vessel tied with doubled C silk just below the second band and about 1 cm distally The area between the ties was thoroughly crushed The dog was able to walk and wag his tail as soon as the anesthesia wore off, but his hind legs seemed a little weak

April 29, 1941 Hind legs are still weak but he can walk, though he wobbles considerably

April 30, 1941 Strength of legs seems to have returned, also dog can wag his tail now Bled for chemistry to day N P N 52 sugar 86 chlorides 422.4

May 5, 1941 Blood pressure right carotid 220 Mm Hg, left femoral 100 Mm Hg Liver function test 5 minutes 20 per cent 30 minutes trace

May 7, 1941 Kidney function test 30 minutes 17 per cent, 60 minutes 40 per cent, total 57 per cent

July 28, 1941 Blood chemistry, N P N 40 chlorides 471 sugar 84

July 30, 1941 Left carotid was moved up just beneath the skin

September 8, 1941 Liver function test 5 minutes, 30 per cent, 30 minutes 0 per cent Blood chemistry N P N 48, chlorides 504.9, sugar 84

September 10, 1941 Pressure left carotid 207 Mm Hg pressure right femoral 140 Mm Hg Kidney function test 15 minutes, 40 per cent 60 minutes, 12 per cent total 52 per cent

September 24, 1941 Examination of this dog's eyegrounds during the summer of 1941, by Doctor Walsh of the Wilmer Clinic, showed hemorrhage and exudates. The left eye showed a few absorbing exudates and both eyes showed many narrow vessels. The nerve heads were normal in color and vision seemed normal.



FIG 4—Roentgenogram of collateral circulation of Dog No 30 injected with modified Hill's mass. The aorta shows two areas of constriction and then complete interruption for about one inch. The constricted areas are at the sites of the first and second bands. The internal mammary arteries are again carrying most of the collateral blood as in Dog No 16. The posterior branch of one intercostal near the point of division is also very much dilated.

September 29, 1941 Blood chemistry N P N 42 chlorides 488 sugar 85

October 1, 1941 Pressure left carotid 218 Mm Hg, pressure right femoral 148 Mm Hg Liver function test 5 minutes 10 per cent 30 minutes 0 per cent

October 6, 1941 Chest reopened, very few adhesions found. The area of the aorta between the ties seemed calcified and when it was cut felt also as though it was. The lumen was obliterated. The cut ends were tied together by ligatures placed near the previous ties in order to prevent retraction and possible angulation of the intercostals. Dog stood the operation well and was up and walking around within an hour.

October 27, 1941 Animal sacrificed today by injecting modified Hill's mass into the left carotid. One hundred and fifty cc of the solution were used, and the injection was made with a syringe with the animal under anesthesia while being bled from the right jugular vein. Two plain roentgenograms were taken and then stereoscopic films. No gross changes were noted in the organs except evidence of chronic passive congestion in the liver. The aorta above the constriction was greatly thickened but not as much as in Dog No 16. The portion under the bands was replaced by scar tissue, and the section that was tied off was calcified with obliteration of the lumen. The collateral circulation was the same as that in Dog No 16 and is well demonstrated in Figure 4.

DIVISION OF THORACIC AORTA

November 27, 1941 The microscopic sections showed nothing abnormal except that they confirmed the impressions gained by looking at the gross specimens of tissue, as demonstrated in Figure 5

COMMENT

We feel that we have been able to demonstrate a new method which in, at least, a small percentage of cases makes it possible to tie and divide the thoracic aorta and still have the animal survive indefinitely in a normal state

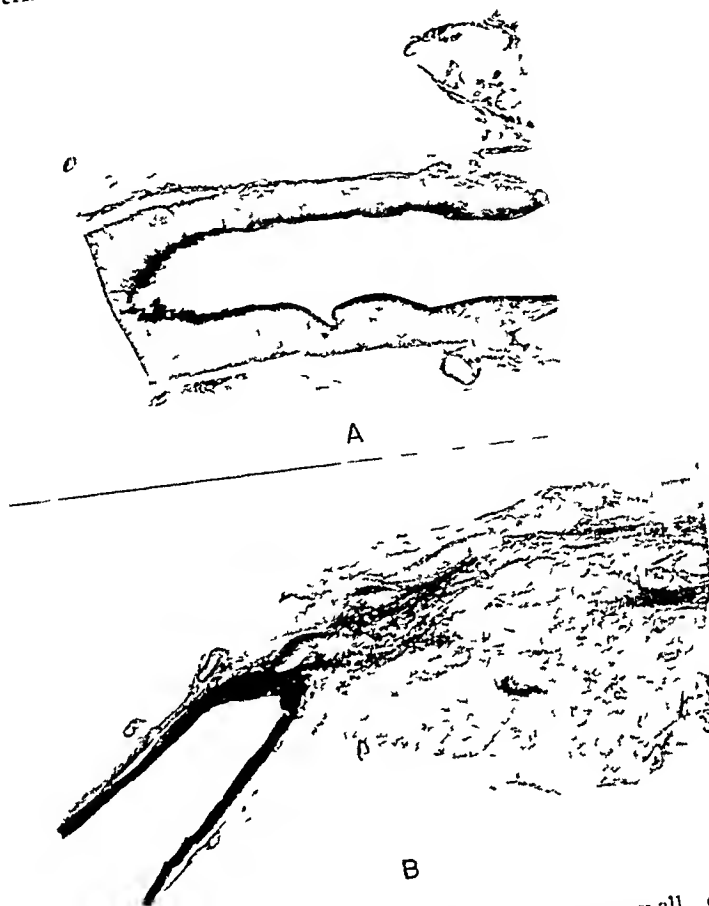


FIG 5—Section (A) was taken from the wall of the aorta of Dog No 30 above the point of division, and Section (B) from below it. Both were cut longitudinally. They demonstrate the same changes in the vessel wall as were shown in Fig 3A.

of health. The physiologic studies made on the two animals reported above, show that there was development of sufficient collateral circulation to allow normal function of the organs below the site of division of the aorta without any demonstrable microscopic changes, except evidence of some chronic passive congestion in the liver. However, the blood pressure above the site of division apparently remains very high for, at least, as long as three years, and may lead to changes in vision as demonstrated by the retinal separation and hemorrhage noted. Therefore, if this method was ever used on a human being this possible complication would have to be kept in mind. We doubt aorta successfully because in cases of aneurysm, which would be about the only indication for its use the vessel wall would probably be so diseased that it would be almost certain to be cut through. In instances in which the remaining portion of the vascular system is normal, this objection would not

apply One band placed fairly close to the aneurysm might slow the circulation enough to produce thrombosis, which would probably be all that would be necessary The method affords a very good means of studying the effect of hypertension on the heart and other structures above the point of division It would also probably be very interesting to study the blood pressures below the point of constriction shortly after it was produced, in order to see whether it is low enough to cause disturbance in the function of the organs below the diaphragm The pressure certainly seemed very low and yet the animals did not show any apparent disturbance of function No physiologic studies were made early on any of the animals because we had no idea which ones would live and did not have time to study them all We were not able to develop any certain means of determining just exactly when an animal would stand ligation of the aorta This is well illustrated by the fact that 20 animals were carried to the point where we thought ligation would be safe, but only six actually survived it for any appreciable length of time, and two of these were paralyzed in the hind quarters It might be that if we had carefully measured the pressure in the femoral artery throughout the course of the experiments we would have been able to tell for certain when sufficient collateral circulation had developed If I were going to repeat the experiments, I would unquestionably do this By using wide bands of best quality rubber we were able to produce collateral circulation of sufficient degree within three to four months We were never able to get an animal to survive after dividing the aorta as a primary procedure even when there seemed to be sufficient circulation below the constrictions We found that it was necessary to ligate the vessel in two separate places and to crush the wall between the ligatures in order to get complete occlusion, because a single tie would either cut through the vessel wall or else the lumen of the vessel would become widened after the ligature had cut down to the intima We wish to stress again the fact that after the vessel is divided the cut ends must not be allowed to retract, because through angulation of the intercostals or some other derangement the collateral circulation is so embarrassed that death will result This technic could be used on any large blood vessel in the body when it is the wish of the operator to produce good collateral circulation distally before he ties or divides it

We wish to thank Dr Rudolph Matas⁷ for presenting the preliminary report on this work, and Drs Mont Reid and Herman Pearse for their interest in it The microscopic sections were reviewed by Dr Arnold Rich, of the Department of Pathology, for which we are very grateful

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article by Dr H E Pearse ⁴)

DISCUSSION—DR HARVEY B STONE (Baltimore, Md) I do not know anything about this subject, but would like to say a word of approbation and appreciation of this perfectly beautiful, long-continued, difficult work just presented so sincerely and convincingly by Doctor Owings I cannot help but feel that he has made a very real contribution to the whole question of the control of circulation by surgical means Whether this particular procedure may be applicable to the human aorta or not, he has clearly designated a number of principles, and he has introduced at least one or two conceptions of the mechanism necessary to be observed in any such procedure So far as I know, no one else has called attention to the fact that the division of an occluded vessel may defeat the purpose of the experiment by releasing the upper proximal stump and permitting kinking of the vessels that carry on the collateral circulation, and if there were no other contribution than this I think that would be very valuable

I have been following his work for a number of years and can assure you there has never been a more honest and sincere and painstaking piece of scientific investigation

DR BARNEY BROOKS (Nashville, Tenn) The experience of Doctor Gage demonstrates again the uncertainty of the obstruction of a large artery by ligation in continuity In a case I reported some 20 years ago, in which the aorta was completely occluded, after ligation in continuity proximal to a large aortic aneurysm, I believe we were correct in ascribing the success of the ligation in apparent continuity to the fact that the ligation was not in reality in continuity, because in the dilatation of the aneurysmal sac, both common iliac arteries had been obliterated and we were, therefore, dealing with what amounted to a terminal aneurysm

The paper of Doctor Owings is a beautiful demonstration of a quality, unfortunately, not frequently found among medical investigators, particularly surgeons His paper is in sharp contrast to those frequently heard in which the results of operation are reported much too soon to be of lasting value Doctor Owings has demonstrated remarkable ability to carry on a single experiment, not for hours, days or weeks, but for years For this sort of investigation he is to be commended

The fact that he found hypertension after ligation of the aorta is opposite to the results which we obtained and published several years ago In our experiments however, the ligature was placed distal to the renal arteries In his experiments, the ligature is proximal to the renal arteries, and I wonder if the hypertension which developed was not in reality because of the influence upon the renal circulation similar to that produced by the Goldblatt clamp Also, I would like to point out that he spoke simply of "blood pressure" I should like to call attention to the fact that numerous investigators, particularly workers on shock and hypertension, apparently measure only mean or systolic pressure One is not always sure which of these is meant, and in

reality "blood pressure" is only significant when both systolic and diastolic pressures are measured

DR JAMES C OWINGS (Baltimore, Md, closing) In answer to Doctor Brooks' question, I wish to say that all the pressures reported were systolic. They were taken by inserting a small needle, connected directly to a mercury manometer, into the lumen of the vessel. It would have been better, of course, to have recorded systolic, diastolic, and mean pressures. If we do further work we shall obtain all three. The production of hypertension in the upper segment is probably on the basis that Doctor Brooks suggested, that is, due to anemia of the kidneys produced by constriction of the aorta, giving the same effect as Goldblatt obtained by pressure on the renal arteries. However, kidney function was normal and microscopic sections of the kidneys showed no change in the tissue in spite of the fact that the pressure in the upper segments was still high at the time the animals were sacrificed.

Doctor Pileoleau asked what happened to the rubber bands. Nothing happens to them except that they tend to migrate through the wall of the aorta as the layers of the vessel wall are destroyed by pressure and are replaced by scar tissue around the outside of the band. If the scar tissue does not develop fast enough, the bands may cut through and cause the death of the animal by hemorrhage. The rubber maintains its elasticity.

Finally, it is well to remember that in ligating the aorta two ligatures must be used and applied some distance apart. The vessel wall between the ligatures must be crushed in order to promote thrombosis and later fibrosis. If this is not done the lumen of the vessel will be reestablished as the ligatures cause atrophy of the vessel wall.

DR MIMS GAGE (New Orleans, La, closing) I would like to congratulate Doctor Owings on his excellent scientific presentation. It is the first time that gradual occlusion, with subsequent obliteration, of the aorta has been accomplished in the experimental animal. However, I should like to make it very clear that one cannot compare the dog's aorta to the human aorta. The dog's aorta is only comparable in size to the external iliac artery of the human, which latter artery can be ligated with comparative safety. The thoracic aorta is different because vital function of both the kidneys and gastro-intestinal tract is dependent upon its potency. Therefore, sudden occlusion of the thoracic aorta by ligature usually ends in disaster, either at the site of the ligature, or more likely in complete suppression of functions of both kidney and intestinal tract.

By the method of gradual occlusion, as demonstrated by Doctor Owings, the functional capacity of the anatomic organs is maintained by the development of an adequate collateral circulation. I do not believe that sudden occlusion of the abdominal aorta by cotton tape will result in permanent obliteration of the lumen. All cases that have survived ligation with tape have demonstrated, both clinically and at autopsy, that the lumen has been partially restored. The aluminum band cannot be used on the human aorta for the purpose of either gradual or sudden occlusion because it will always cut through, resulting in fatal hemorrhage. Therefore, if we can gradually occlude the aorta to a narrow tube by the method presented by Doctor Owings, we then can ligate the diminished aorta with success. The aorta will then be permanently obliterated.

Doctor Matas recently told me that he thought Doctor Owings' method of gradual occlusion was one of the greatest surgical contributions to surgery of the thoracic aorta. As the method has not been tried on the human aorta, we will have to wait before passing judgment on its clinical applicability.

GAS GANGRENE*

REVIEW OF SEVENTY-ONE CASES

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IN DISCUSSING GAS GANGRENE, several variable factors must be considered. The incidence and, to a lesser extent, the virulence appear to vary with time and locality.

Gas gangrene was relatively unknown during the Civil War, and Keen¹ did not see a gas infection during his entire service. On the other hand, the trench warfare of World War I offered optimum conditions for the development of gas gangrene, and Taylor² demonstrated the Welch bacillus in 70 per cent of wounds cultured during this period. Thus far there have been few cases reported during the present war.

When we turn to civil life, we find this same variation in incidence in different parts of the country. While there has been a definite increase in gas gangrene during the past 15 years, probably due largely to the increased number of automobile accidents, this increase has been more evident along the Eastern seaboard than in the deep South or middle West. The State of Virginia is in the unenviable position of reporting more cases of civil gas gangrene than any other locality of comparable population.

In 1900, Welch³ was able to collect only 46 cases of proven gas bacillus infections and 14 of these were reported abroad. During the past ten years almost twice this number of cases have been seen in the Medical College of Virginia Hospitals alone. In 1926, Bellevue Hospital⁴ reported one case of gas gangrene for every 7,310 admissions. During the past decade, one out of every 1,342 admissions at the Medical College of Virginia Hospitals had gas gangrene on admission or developed it during the hospital stay. Newell,⁵ of Chattanooga, on the other hand, found only five gas infections in more than 42,000 traumatic cases during the past 21 years. He suggests that "porous, sandy, hilly soil does not harbor organisms as does flat country." Whatever the cause, it is interesting to note that the incidence of gas gangrene at the University of Virginia Hospital is almost identical with that at the Medical College of Virginia.⁶

The reported mortality from this condition has been more constant. One thousand, three hundred and eighty-nine cases occurred in the American Expeditionary Force, with 674 deaths, a mortality of 48.5 per cent.⁷

Ghormley,⁸ in 1935, reported 33 cases occurring at the Mayo Clinic, with a mortality of 42.5 per cent.

Callender⁹ and his associates collected 109 cases encountered at the San Francisco Hospital from 1919 to 1936 with a mortality of 51.8 per cent. He also reported 12 subsequent cases treated with iontophoresis, with only

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one death, but stated he was omitting several other fatal cases from this latter series because of marked arteriosclerosis

Maes¹⁰ recently reviewed 73 cases of gas gangrene treated in the Charity Hospital in New Orleans during the past ten years, with a mortality of 38.4 per cent. During this same period 341 cases of tetanus were seen in the Charity Hospital. Tetanus is rarely seen in Virginia, and no instance of this infection occurred in conjunction with gas gangrene.

The lowest mortality reported was that of Kelly, Dowell, Russum and Cohen,¹¹ who collected a series of 132 cases treated by roentgenotherapy, with only 15 deaths, a mortality of 11.3 per cent. A careful review of this article, however, shows that ten additional cases, mentioned at the onset, are not included in the final tabulation, and if they, too, were unfavorable cases, the mortality would be considerably increased.

A further drawback in this series was the method used in gathering this data. The 142 cases were reported by about 100 physicians, and thus represent an average of less than two cases per physician. This is hardly a fair basis of comparison. To digress further for a moment, a comparison should be made between the type of gas gangrene seen in Virginia and that reported in this article. Doctor Kelly states that a patient who receives roentgenotherapy during the first 24 hours after the infection is recognized as an "early case," and 100 per cent of these patients should recover. It has been our unpleasant experience to have patients die within less than 24 hours after the infection was recognized clinically. He also states that a patient with gas gangrene should receive two roentgen ray treatments daily for three or possibly five days, and that one who has not received this amount of radiation has not been properly treated. We have found that a patient who survives 72 hours is usually well along the road to recovery, for most of our fatalities occurred within the first three days. These facts are mentioned in order to bring out a point that has been raised by others, namely, that Doctor Kelly may be treating a less virulent type of gas gangrene in the middle West than that encountered in the East.

A source of error in comparing mortality following different types of treatment has been the tendency of some authors to omit certain cases from their tabulations. This is particularly noticeable when some special mode of therapy is advocated. It is not uncommon, for example, to find patients who were moribund on admission, who had preexisting gangrene, marked arteriosclerosis, diabetes or so-called "gas infections" omitted for the summary, and thus a misleading impression may be given concerning the actual mortality.

With this thought in mind, a study has been made of all cases of gas gangrene treated at the Medical College of Virginia Hospitals during the past ten years. This period, from January 1, 1931, through December 31, 1940, was chosen, as it coincides with the present methods of diagnosis and filing charts. All cases with a positive bacteriologic diagnosis of *C. welchii*, which also showed evidences of a gas infection, and all patients with unmis-

takable clinical or autopsy evidence of this condition, were included in this study

A study of this type is misleading in that some of these patients died of the associated injuries or disease, and the gas infection was of secondary importance, or nonexistent, at the time of death. It would be more misleading, however, to attempt to separate these cases, and I believe the gross figures are of more worth in evaluating the various types of treatment.

Seventy-one cases of gas gangrene were treated at the Medical College of Virginia Hospitals, and 21 died, a mortality of 30.9 per cent. The number of cases has been remarkably constant—36 during the first five years, and 35 during the last five years. The mortality, however, has increased, only eight patients died during the first five years, whereas 14 died during the second corresponding period. This was an increase of 75 per cent, despite the employment of additional therapeutic measures during this latter period.

The treatment during this decade corresponded to that followed generally, with the exception that prophylactic perfringens antitoxin was probably given more freely here than elsewhere, and sulfanilamide was used locally very early at the Medical College of Virginia Hospitals.

In 1931, nine cases of gas gangrene of the extremities were treated, chiefly by amputation and without perfringens antitoxin, only one patient died, a mortality of 11 per cent.

During the next four years, a prophylactic dose of perfringens antitoxin was usually administered to the traumatic cases, and large doses of antitoxin were given therapeutically. Débridements were performed more frequently than amputations. Twenty-seven cases were treated, and seven died, a mortality of 26 per cent. In fairness to this method, it should be stated that four of these deaths followed gas gangrene originating in the trunk. If only the cases were included in which the gas gangrene originated in an extremity, the mortality would be exactly the same as in the first year of the tabulation, namely, 11 per cent.

During the past five years, larger prophylactic and therapeutic doses of perfringens antitoxin were given. Roentgenotherapy was utilized frequently both prophylactically and therapeutically, and during the past two years many of these cases received sulfanilamide locally and generally, in addition to the usual surgical measures of débridement and amputation. Despite the intensity of this treatment, the mortality has been distressingly high—35 cases were treated, with 14 deaths, a mortality of 40 per cent. Four of the five cases with involvement of the trunk died. Even if we omit these cases from our tabulation, the mortality from gas gangrene of the extremities was 33.3 per cent, or three times that of the corresponding infections during the first five-year period. A careful search was made in an effort to explain this high mortality. Some of these patients had associated injuries or disease, that virtually precluded their recovery, but this was also true in our earlier cases. A possible explanation, in part, is found in the age distribution in the two five-year series. Only two patients were over age 60 in the first

TABLE I
RESUMÉ OF CASES

Year	Patient	Race	Sex	Age	Cause	Operation	X-ray	Anti-toxin	Culture	Days in Hosp	Result
1931	H S	C	M	28	Electrical burn	Amputation			C <i>welchii</i>	40	Imp
31	C M	C	F	52	Nail wound	Amputation			C <i>welchii</i>	14	Imp
31	J W	C	M	54	Ulcer Diabetic	Amputation			C <i>welchii</i>	96	Imp
31	B J	C	M	34	Human bite	Amputation				14	Imp
31	B S	C	M	34	Shotgun wound	Amputation			C <i>welchii</i>	14	Imp
31	N C	C	M	52	Comp fracture	Amputation				2	Died
31	H C	C	M	20	Shotgun wound	Debridement			C <i>welchii</i>	58	Well
31	W T	W	M	43	Crushing injury	Amputation			C <i>welchii</i>	50	Imp
31	J W	C	M	49	Comp fracture	Amputation				35	Imp
1932	W F	C	M	24	Shotgun wound	Débridement		P & F	C <i>welchii</i>	45	Well
32	J C	W	M	13	Crushing injury	Débridement		P & F	C <i>welchii</i>	48	Well
32	C M	W	M	32	Comp fracture	Amputation		F		28	Imp
32	B B	C	F	36	Tubo ovarian abscess	Drainage		F	C <i>welchii</i>	36	Died
1933	M B	C	F	6	Crushing injury	Débridement		P & F	C <i>welchii</i>	21	Well
33	J H	C	M	42	Shotgun wound	Débridement		P & F	C <i>welchii</i>	55	Well
33	J L	C	M	25	Stab wound	Debridement		F	C <i>welchii</i>	94	Well
33	N I	C	M	16	Comp fracture	Debridement		F	C <i>welchii</i>	195	Well
1934	R B	C	M	22	Comp fracture	Amputation		P & F	C <i>welchii</i>	82	Imp
34	J W	C	M	32	Shotgun wound	Débridement		P & F	C <i>welchii</i>	54	Well
34	J M	W	M	45	Shotgun wound	Débridement		F	C <i>welchii</i>	44	Well
34	E C	W	M	33	Crushing injury	Débridement		P & F	C <i>welchii</i>	60	Well
34	G R	W	M	47	Comp fracture	Débridement		P & F	C <i>welchii</i>	3	Died
34	W A	C	M	5	Comp fracture	Amputation		P & T	C <i>welchii</i>	102	Imp
34	D F	C	M	20	Shotgun wound	Débridement		P & F	C <i>welchii</i>	57	Well
34	E B	C	M	10	Comp fracture	Débridement		F	C <i>welchii</i>	150	Well
34	D S	C	M	48	Shotgun wound	Débridement		P & F	C <i>welchii</i>	4	Died
34	E J	C	M	28	Perforated ulcer	Incision and Drainage		F	C <i>welchii</i>	7	Died
34	M L	W	F	73	Diabetic gangrene	Post amputation			C <i>welchii</i>	3	Died
34	F S	C	M	39	Perforated appendix	Incision and drainage		T	C <i>welchii</i>	5	Died
'34	B I	W	M	53	Embolie gangrene	Amputation		F	C <i>welchii</i>	44	Imp
1935	P G	W	M	60	Amputation for cancer	Debridement		F	C <i>welchii</i>	35	Well
35	J H	C	M	50	Crushing injury	Debridement		P & T	C <i>welchii</i>	18	Well
35	B W	W	M	21	Shotgun wound	Débridement		P & T	C <i>welchii</i>	13	Well
35	F M	C	M	65	Diabetic gangrene	Post amputation		P		8	Died
35	J B	C	M	16	Shotgun wound	Debridement		P & T		122	Imp
35	E R	C	F	36	Infected incision	Drainage		F		6	Died
1936	W R	C	M	19	Stab wound artery	Amputation		T		59	Imp
36	C P	W	M	24	Comp fracture	Amputation		P & T	C <i>welchii</i>	55	Imp
36	H V	W	M	40	Thrombosis artery	Amputation		T		17	Died
'36	S T	C	M	72	Shotgun wound	Amputation		P		24	Imp
36	T C	C	M	64	Amputation gangrene	Débridement		F		13	Died
36	G H	W	M	49	Amputation Buerger's	Reamputation	+	T	C <i>welchii</i>	48	Imp
36	J F	C	M	32	Comp fracture	Amputation	+	P & F		29	Imp
36	W A	C	M	35	Shotgun wound	Amputation		P & T		42	Imp
1937	E G	C	M	10	Comp fracture	Amputation		P & T		49	Imp
37	C D	W	M	22	Gun shot wound	Amputation		T		31	Imp
37	E M	C	M	26	Comp fracture	Sulfanilamide Débridement	+	P & T		59	Well

TABLE I (Continued)

Year	Patient	Race	Sex	Age	Cause	Operation	X-ray	Anti-toxin T	Culture	Days in Hosp	Result
'37	C B	C	M	19	Traumatic amputation	Débridement		T		52	Imp
37	E S	W	M	34	Shotgun wound	Débridement	+	P & T		2	Died
1938	A B	C	M	67	Infected burns	Bilateral amputation		T	C <i>welchii</i>	5	Died
'38	G M	W	M	62	Comp fracture	Amputation	+	T	C <i>welchii</i>	166	Imp
38	M S	C	M	22	Bilateral gangrene	Bilateral amputation		T		8	Died
38	L S	W	M	20	Comp fracture	Sulfanilamide Débridement		P & T	C <i>welchii</i>	3	Died
38	J B	C	M	35	Shotgun wound	Sulfanilamide Débridement		P & T		6	Died
1939	E G	C	M	34	Comp fracture	Amputation	+	P & T	C <i>welchii</i>	15	Died
39	T S	W	M	63	Comp fracture			P	C <i>welchii</i>	2	Died
39	W B	C	M	17	Shotgun wound	Sulfanilamide Débridement	+	P & T		117	Well
39	W W	C	M	30	Comp fracture	Sulfanilamide Drainage	+	P & T	C <i>welchii</i>	190	Well
'39	C H	C	M	27	Perforated ulcer	Sulfanilamide		P	C <i>welchii</i>	6	Died
39	H B	C	M	17	Shotgun wound	Incision and drainage	+	P & T	C <i>welchii</i>	10	Died
39	L P	W	M	37	Comp fracture	Amputation	+	P & T	C <i>welchii</i>	102	Imp
39	G C	W	F	26	Comp fracture	Sulfanilamide Amputation	+	P & T	C <i>welchii</i>	56	Imp
39	H M	W	M	37	Traumatic gangrene	Amputation	+	T		153	Imp
1940	L W	C	F	31	Traumatic gangrene	Amputation Sulfanilamide	+	P & T	C <i>welchii</i>	34	Imp
40	D B	W	M	45	Comp fracture	Sulfanilamide Amputation	+	P & T	C <i>welchii</i>	77	Imp
40	N P	C	M	23	Crushing injury	Sulfanilamide	+	T	C <i>welchii</i>	4	Died
40	A B	W	F	65	Hypodermic	Débridement	+	T	C <i>welchii</i>	35	Died
40	H C	C	M	64	Bilateral gangrene	Amputation	+	T	C <i>welchii</i>	2	Died
40	L F	C	M	18	Comp fracture	Sulfanilamide Amputation		P & T		33	Imp
40	C J	W	M	16	Comp fracture	Sulfanilamide Débridement	+	P & T	C <i>welchii</i>	70	Imp
'40	E B	C	M	26	Shotgun wound	Sulfanilamide Drainage		P & T	C <i>welchii</i>	52	Imp

KEY P = Prophylactic
 T = Therapeutic

Well = Recovery without loss of extremity

Imp = Recovery with loss of extremity

series, while seven patients over age 60 were found in the second period. The mortality for all patients past age 60 was 77.7 per cent. A second, and more disturbing explanation may be that the introduction of chemotherapy in some instances may have beguiled the surgeon into a false sense of security and he may have relaxed, unconsciously, in his effort to perform a thorough débridement of recent wounds.

A study has been made of the various preventive and curative measures used in the treatment of gas gangrene at the Medical College of Virginia. The various types of treatment will, of necessity, be considered separately, although they were usually used in conjunction with other forms of therapy.

Thirty-seven patients who subsequently developed gas gangrene received perfingens antitoxin prophylactically—ten died, a mortality of 27 per cent.

Thirty-four patients who had not received perfringens antitoxin prophylactically developed gas gangrene, and 12 died, a mortality of 35.5 per cent. Superficially, this would appear to indicate that gas gangrene ran a milder course and was more amenable to treatment if antitoxin was given prior to the clinical onset of the infection. Two facts argue against this interpretation. The patient who did not receive perfringens antitoxin as a prophylactic measure was usually either admitted after the onset of gas gangrene or the possibility of gas gangrene was not considered until the infection was evident, and sometimes advanced. The patient who developed unsuspected gas gangrene, as a rule, had a serious associated condition, such as diabetes, a preexisting gangrene, or a perforation of the gastro-intestinal tract.

A second method of evaluating the value of perfringens antitoxin may be found in the various numbers of units given in this series. Nineteen patients were given the so-called prophylactic dose of perfringens antitoxin, which represented 1,000, 1,500, or 2,000 units, depending upon the maker and the method of standardization (average dose was 1,579 U). The mortality in these cases was 26.3 per cent. On the theory that if a small prophylactic dose was beneficial, a larger dose should be more helpful, our routine was then changed and a therapeutic dose of 10,000 units, or more, was given as a prophylactic measure to 17 cases. Five patients also died in this series, a mortality of 29.4 per cent. In other words, the mortality was slightly higher after a large prophylactic dose than after a small one. Two patients received 30,000 units, or 15 times the recommended prophylactic dose, and both developed gas gangrene, with death in one case.

Unfortunately, data are not available concerning the total number of patients who received perfringens antitoxin prophylactically, in terms of the number who later developed gas gangrene, but the above figures arouse doubt as to the value of antitoxin as a preventive measure. Pursuing this thought further, it is hard to see how a massive infection could be cured by antitoxin given therapeutically if a prophylactic injection of antitoxin could not prevent the infection at its inception.

Fifty-seven patients received an average of 31,560 units of perfringens antitoxin therapeutically, and 17 died, a mortality of 30.9 per cent.

Twelve patients received sulfanilamide locally as a precautionary measure, or orally as a therapeutic procedure, and four died, or 33.3 per cent.

Eighteen patients received roentgenotherapy as a prophylactic and/or therapeutic measure, and six died, again, a mortality of 33.3 per cent. Encouraging, however, is the fact that 35 patients were given roentgenotherapy prophylactically who failed to develop gas gangrene.

The operative therapy fell naturally into two groups, namely, amputation of involved extremities, or debridement, with excision of infected muscle bundles. Thirty-six limbs were amputated with six deaths, with a mortality of 18.2 per cent. Twenty-eight debridements were undertaken, with eight deaths, a mortality of 28.5 per cent.

To summarize, the following prophylactic and therapeutic procedures were used in the treatment of gas gangrene, with the indicated mortality

Roentgenotherapy (prophylactic and/or therapeutic)	33 3%
Therapeutic perfringens antitoxin	30 9%
Sulfanilamide (locally and/or generally)	30 8%
Prophylactic (10 000 U) perfringens antitoxin	29 3%
Débridement	28 5%
Prophylactic (1,000-2,000 U) perfringens antitoxin	26 3%
Amputation	18 2%

Despite this inconclusive evidence, we have felt it necessary to formulate a uniform method for treating these cases, and the following outline, based on our experience and that of others, has been evolved

In addition to the usual care that all traumatic cases should receive, every case in which the deep fascia is penetrated is considered a potential gas bacillus infection and treated accordingly. This includes a painstaking clean-up with sterile water, green soap and shaving, followed by ether, iodine, and alcohol. The operative field is draped, and a purposeful débridement is undertaken. No nonessential tissue that has been exposed by the injury is permitted to remain. It is imperative that the full extent of the wound be determined and explored. The under surface of the extremity must be inspected for additional injuries or wounds of exit. All foreign material and devitalized bone is, of necessity, sought and removed. The original instruments are discarded.

Muscle removed from the wound should be cultured for gas organisms. I cannot leave this phase of the treatment without emphasizing again the importance of the débridement. Ultimate success or failure hinges more upon this than any other aspect of the therapy. A copious warm normal saline irrigation is then used, care being taken that all parts of the wound are flooded with solution. After ligating all bleeding points, 10 Gm of sulfanilamide crystals are placed in the wound if the incision is to be closed. Twice this amount may be used if the incision is to be packed open. Correspondingly smaller amounts should be used in children. The decision as to whether the incision should be closed rests upon so many considerations that I shall only say that if the edges cannot be approximated without tension, or if a dead space remains, the wound is left open, with an abundant gauze pack. If a fracture is present or if the wound is near a joint, the part is immobilized by an adequate plaster encasement. Fifteen hundred units of tetanus antitoxin are injected. A prophylactic or therapeutic dose of perfringens antitoxin may be given, if the operator has faith in this agent. If there is any impairment of the circulation to the part, a sympathetic novocain injection should be given. Henry¹² does this routinely in all potential cases of gas gangrene.

As soon as possible, on the day of operation, a postoperative roentgenogram is taken. This checks the position of the fragments if a fracture is present, and serves as a standard for comparison when later roentgenograms are made to determine if gas is present in the tissues. A prophylactic roentgen

ray treatment, as outlined by Kelly,¹¹ should also be given to the involved area at this time. Twelve hours later, another film is made to determine if gas has increased in the damaged area, and a second prophylactic roentgen ray treatment should be given. A third roentgenogram, made 24 hours after the injury, will definitely determine if a gas infection is present. If this is negative, there is little likelihood that gas gangrene will occur. Six grams of sulfanilamide, or sulfathiazole, should be given daily for the first 48 or 72 hours during this probationary period. The clinical signs and symptoms meanwhile should not be neglected, and excessive pain, swelling, tachycardia, discoloration, or crepitus should point to a gas infection. The roentgenologic diagnosis, however, can and should be made before these changes are evident. If gas gangrene develops, an immediate debridement, or open amputation, should be performed, depending upon the degree of involvement and the state of the circulation distal to the infection. Roentgenotherapy and the sulfonamides should be continued. An erythrocyte count and hemoglobin determination should be made daily, followed by blood transfusions as indicated for these patients frequently develop a rapid and severe secondary anemia. An electrocardiogram should be made before the patient leaves the hospital, for severe myocardial damage has been reported following gas infection.

In the above treatment an attempt has been made to combine the best elements in our own experience with those suggestions, made by others, that seem to offer the greatest likelihood of success. While it is too early to draw any conclusions as to its ultimate worth, we feel encouraged and justified in continuing this method.

CONCLUSIONS

The incidence of gas gangrene continues high in Virginia, despite active measures directed toward its prevention.

No single agent or drug has proved specific in treating this condition.

In our experience perfringens antitoxin has been disappointing both prophylactically and therapeutically.

The introduction of the sulfonamides may have caused some operators to be less careful in their debridement of wounds and thus, in part, may explain some of our recent failures in preventing and treating this condition.

In traumatic cases an early, painstaking debridement is of greater value than any other procedure in preventing gas gangrene.

We have been unable to evaluate the worth of prophylactic and therapeutic roentgenotherapy, but do feel that it is helpful as an early diagnostic measure.

A suggested method of treatment is offered.

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DISCUSSION—DR E DUNBAR NEWELL (Chattanooga, Tenn) I think this paper is very timely In 1938, I read a paper on this subject before this Association, and at that time I said the reason I was doing so was because I had a case of gas gangrene, and I thought I was familiar with it at that time After I had this case, I read the literature and found I knew nothing about it

There are a few things to stress distinctly The first is that the incidence of gas gangrene infection varies markedly in different localities But that does not have anything to do with the present status, because we will most likely have a million men in other fields within a year, and we must consider that we will have gas gangrene infections following the soldiers Treatment begins when you first see the patient Personally, I do not believe the mortality should be more than 5 or 10 per cent, if adequate treatment is given at once—adequate débridement, proper handling of the wound, and immobilization of the wound at once Prophylactic polyvalent antitoxin probably does some good, but do not depend on it In a series from New Orleans, the mortality was less in the cases in which they gave prophylactic polyvalent antitoxin for three days in succession

To me the most important factor is the early diagnosis of gas gangrene infection That cannot be done by smears and cultures In evacuation hospitals in France we found that practically all cultures showed the *C welchii* and other organisms of that type As a matter of fact, only 60 to 65 per cent of those cases developed gas gangrene So positive cultures and smears do not mean anything

It is important to make an early diagnosis, and you must be more alert and more suspicious in making this diagnosis than were our forces in Honolulu in the present emergency The first thing you notice is pain at the site of the wound When you have a patient with a severely contaminated wound and he develops pain suddenly, look at the dressings, and if there is a sweetish-sour odor, a distinctive odor, and the wound looks a little puffy, and the pulse is high in proportion to the temperature, then take a roentgenogram, and if you see some gas bubbles in the wound, it is your duty to suspect at once that you have a gas gangrene infection, and polyvalent antitoxin should be given every four to ten hours in large doses

DR MIMS GAGE (New Orleans, La) I would like to ask Doctor Warthen if he has noted any seasonal variation in his cases of gas gangrene In

New Orleans we have found the incidence to be higher in the winter months. This is due to the prevalence of wool clothing which harbors the spores of *C welchii*. In 1923-1924 and in 1932 we found that all wool clothing and blankets contained the spores of *C welchii*. The felt wads of shotgun shells also contained *C welchii* spores in 100 per cent of those cultured. We were able to produce gas gangrene in the experimental animal (rabbit) by inserting pieces of wool cloth and pieces of wads from shotgun shells into the traumatized muscles of the rabbit's thigh. The production of gas in the tissues was followed by roentgenographic visualization. In a number of the animals the wound was ruptured by the gas pressure. Therefore, we have believed that bits of wool clothing and wadding from shotgun shells driven into muscle tissue were responsible for the development of gas gangrene in a high percentage of civil cases. This of course would be greatly augmented in war.

The development of gas bacillus infection is dependent upon the presence of devitalized muscle to act as a culture medium. Therefore, one must first have muscle injury resulting in devitalization of muscle tissue. This occurs when the blood supply has been destroyed to a certain portion or portions of a single muscle or a group of muscles. There are certain vulnerable areas in which there is only one blood supply to the muscles of the lower extremity—first, the calf muscles, next, the gluteal region, and third, the thigh. In these areas, if the main artery is severed, traumatized or segmentally becomes spastic, large areas of muscle tissue immediately become ischemic, and the gas bacillus readily and rapidly invades and produces massive gangrene.

If we can eliminate all devitalized muscle, we can prevent the development of gas gangrene. Therefore, I have taught for years that gas bacillus infection is a preventable disease. However, it is so only when the surgeon has a thorough knowledge and practical appreciability of debridement. A good debridement is certainly more difficult of execution than is gastrectomy or colectomy. If one fails to remove all devitalized muscle by debridement, then he has not performed a débridement and the development of gas gangrene frequently takes place.

The use of the sulfonamides in the wounds after debridement seems to act as a protective and preventive measure. I believe that its effect is mainly by producing internal washing away of contaminating anaerobic organisms and coffer-damming the tissue by cellular infiltration. This prevents tissue destruction by the toxins as well as invasion of the tissues by the organisms.

The use of roentgenotherapy is of no benefit as regards specific effect on the organisms of the *Clostridium* group, and I believe it is of no value in treatment of gas gangrene. I sincerely believe that with a thorough knowledge of the bacteriology of gas gangrene, the surgical principles of débridement, with mechanical cleansing from both without and from within, will, in the majority of cases, prevent the development of gas gangrene. If infection has occurred, then it can be minimized or stopped by both surgical excision and local chemotherapy. However, in those cases where many muscles are involved (group or massive gas gangrene), amputation will be the procedure of choice. We must not expect too much from chemotherapy and should never subjugate surgical principles to chemotherapy, but combine both in an intelligent manner.

DR W O BULLOCK (Lexington, Ky.) Referring to the paper given by Doctor FRIED this morning, I noted that sulfasuxidine in the intestinal tract seemed to possess a selective action against anaerobic organisms. It is not improbable that this selective action may occur or may take place elsewhere.

in the body against the anaerobic germs responsible for gas gangrene, and it may well be that in this drug we may have the answer to this distressing problem

DR HOWARD M. CLUTE (Boston, Mass.) Severe gas gangrene infections are most frequently seen in crushing injuries of the extremities. It is true, however, that infection with *C. welchii* has in rare instances followed every type of surgical operation on the abdomen. I have, in recent years, observed three cases, one patient had rupture of the liver with a simple fracture of the ribs, and died of overwhelming gas bacillus infection, the others followed cecostomy and large bowel resection. Each of these recovered following large doses of antitoxin.

It is well known that *C. welchii* inhabits the intestinal tract of most people. If obstruction of the bowel occurs, with the resultant tissue anoxemia, the stage is set for these organisms. It is astonishing that more such infections do not occur in patients with bowel obstruction.

I want to emphasize what Doctor Newell said, with particular reference to abdominal wounds. The successful treatment is largely dependent on early recognition and immediate treatment. The signs are rapid rise of pulse and temperature, and especially pain in the wound, a copper-red color of the skin, and gas in the tissues, which you can hear with the stethoscope as early as you can find it roentgenologically. Smears and cultures confirm the diagnosis, but while waiting for these, active treatment should be undertaken. With gas bacillus antitoxin alone, both our cases with infections of the abdominal wall recovered. I have no doubt that to-day we would give sulfanilamide, but we would use antitoxin as well. It seems to me that in gas bacillus infections more than in any other condition, the surgeon's diagnostic acumen is the important factor in determining the outcome.

DR JULIAN K. QUATTLEBAUM (Savannah, Ga.) I wish to express my appreciation for the privilege of discussing Doctor Warthen's paper. It is my impression that the frequency and virulence of gas bacillus infection certainly varies in different localities. It is not an infrequent occurrence in our section of the country, as I have had some 20 private cases during the past 15 years. We are inclined to associate gas bacillus infection with severe injuries and much damage to muscle tissue. However, this infection can follow a very trivial injury, and in such cases it usually proves fatal.

I have had three cases which followed very minor injuries indeed. The first was a physician who, having misplaced his cuff link, attempted to pin his cuff and punctured his wrist with the pin. Almost immediately a severe infection occurred with great swelling of the arm, intense pain, fever and prostration. We did not recognize this as being a case of gas bacillus infection until the arm was opened a few days later, then the typical odor, bubbles of gas and extensive necrosis of muscle established the diagnosis. This case was interesting in that he had just taken a tub bath and his skin was cleaner than usual when the accident occurred. The patient refused amputation and the arm was thoroughly débrided, but he promptly died. It is unlikely that amputation of the arm would have saved him.

The second case was a man who dropped a stick of stove wood on his foot. He was wearing his shoe at the time and the skin on the dorsum of the foot was barely broken. Within six hours the man was desperately ill, with an area of necrosis, approximately 6 cm. in diameter, surrounding the area of the injury. The remainder of his foot was livid. A few hours later the entire foot was gangrenous and the process had spread above the ankle.

joint A mid thigh amputation was performed, and death occurred less than 12 hours later

The third case was a ten-year-old girl who was bitten high on the thigh by a red-bug The mother attempted to remove the tiny bug with a needle Twelve hours later this area was seminecrotic and the child was very ill The infection spread rapidly, involving the vulva, lower abdominal wall and the right leg above the knee Although massive doses of perfringens antitoxin were given and extensive debridement undertaken, the fatal outcome was not long delayed

It is my opinion that cases of gas bacillus infection such as these are incurable from the beginning Other cases respond to treatment and get well I have seen the infection stopped promptly and recovery take place following a shoulder joint amputation, when the gangrenous process was within a few inches of the joint itself At times the infection is limited to one muscle or a group of muscles, and is apparently confined by the muscle sheath, and can be cured by simply excising the involved muscles No doubt the shock of amputation has contributed to the fatal outcome in some cases and, certainly, it will not always stop the advance of the infection However, if the infection is in a limb so badly crushed or mangled as to greatly impair its usefulness should recovery be possible, I think immediate amputation is the treatment of choice The stump should be left open and negative cultures should be obtained before secondary closure is attempted, as recurrence in the closed stump has occurred in my experience Roentgenotherapy and the sulfonamide drugs have been used in the treatment of practically everything else, and may be of value in the therapy of gas bacillus infection In this connection I am reminded of the man who, being notified of his mother-in-law's death, was asked to advise whether she should be embalmed, buried or cremated He replied "Take no chances, use all three" So in cases of genuine gas bacillus infection give it everything you have

DR HARRY J WARTHEN (Richmond, Va, closing) The treatment we have followed since we have found our mortality was increasing was debridement—thorough debridement, painstaking débridement In addition to that we use roentgenotherapy prophylactically We give the prophylactic dose recommended by Kelly Each time we give a treatment we take a roentgenogram of the area to see if there is increase in the gas We feel that diagnosis can be made earlier by roentgenography than by any other method

Doctor Gage asked about seasonal variation We looked for that, but in Virginia it seems to develop under any conditions and we could not find anything significant

IMPROVED METHODS IN EXTREMITY AMPUTATIONS FOR DIABETIC GANGRENE*

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THE SENIOR AUTHOR desires to present two modifications of technic which have been instituted at the City Hospital, New York, to reduce the mortality in mid thigh amputations for either arteriosclerotic or diabetic gangrene. These procedures are: First, the sleeve operation for amputations above the knee, and, second, the refrigeration method of anesthesia.

No claim is made to any originality with either procedure, but it has been our privilege to watch and, to some extent, to participate in these procedures, and, therefore, we feel that a thorough evaluation of the operative methods and the end-results may be made.

The City Hospital, New York, receives the poorest risk patients of the metropolitan area. Ambulances of the various city hospitals may take patients either to their own hospitals or to the Metropolitan or City Hospital on Welfare Island. Each of these two hospitals receives on alternate days.

There are two factors, therefore, that militate against good statistics. Frequently an ambulance surgeon picks up an elderly diabetic with gangrene, and, in order not to overcrowd his own hospital, he takes this patient to Welfare Island. The patient is usually a poor risk. Secondly, it is difficult, or impossible, to have an adequate nursing staff at the City Hospital, because nurses object to living on the island. This tends toward inadequate nursing of the sick patient.

We propose to limit this discussion of amputations to those above the knee, as it is this group that presents the highest morbidity and mortality figures. It is necessary, before stating our mortality, to present the conditions noted above, for it is unfair to compare the results of these underfed, elderly patients with the better economic- and age-groups in the voluntary hospitals. In order not to cloud the issue, the figures of the City Hospital series will be the basis of this discussion.

Finley, in 1937, analyzed the series of mid thigh amputations at the City Hospital. There were 57 cases with 31 deaths, a mortality of 54.4 per cent. From 1938 to 1941, there were 63 amputations with 39 deaths, a mortality of 62 per cent. During these years there was not a well-organized peripheral-vascular service, and many operators performed many types of amputations, but the guillotine or the modified anterior and posterior flap method was used the most frequently. Three years ago the peripheral-vascular surgical group

* Read before the Southern Surgical Association, Pinchurst, N C, December 9-11, 1941.

was assigned to Dr Lyman Crossman, and under his efficient direction progress became immediately apparent

The senior author has observed the excellent results at the Veterans' Hospital, where Fuller had worked out a modification of the Callender operation, with particular reference toward preserving the collateral superficial blood supply about the knee, and, second, the production of a well-padded stump adapted for an artificial leg

This operation was introduced at the City Hospital and has been adopted, with a few modifications, by the peripheral-vascular service under Crossman's direction

Following are the details of the technic as practiced by Fuller. A circular incision is made at the level of the insertion of the patella tendon in the tubercle of the tibia. The skin and fascia are incised in the primary incision, and, as they are incised they are held together by skin clips in order to prevent subcutaneous fat separating from the fascial sheath. This technic is carried out in the entire circumference of the extremity, completely dividing the fascial envelope and skin together. The patella tendon is then transected above its insertion to the tibial tubercle, following this the biceps tendon is cut near its insertion at the head of the fibula, exposing the lateral border of the popliteal space. If no tourniquet is used, the finger is inserted into the floor of the popliteal space through the loose areolar tissues, and the vessels and nerves are lifted from the floor of this space. A tape is passed around the vessels and tied securely. The vessels are clamped distal to the tape and the vessels and nerves cut. The lateral hamstring tendons are then transected. A towel clip is then placed on the divided patella tendon and the anterior aspect of the flap is raised, revealing the ramifications of the quadriceps bursa.

From this point forward, all structures are sleeved-out, using a Mayo dissecting scissors and closely following the margins of the femur. With the index finger of the left hand, to guide the scissors, the fascial attachments along the epicondylar ridge and the femur itself are separated. This coming-out process is carried out until all fascial attachments of the femur are freed to the desired level, preferably the junction of the middle with the lower third of the femur, well above the condyle. The muscle is then protected either by moist towels or with a metal cuff, and a Gigli saw placed about the shaft of the femur. The femur is then transected, the towel or guard removed, and the entire skin and muscle allowed to drop back over the end of the femur. At this stage the vessels which have been grasped earlier by the tape may be individually isolated, ligated and cut. The sciatic nerve is identified, dissected upward, injected with alcohol, and ligated. The patella is excised from the patellar tendon and the wound allowed to drop back together. The clips which join the fascia to the skin are removed, the fascia is loosely sutured, and, if there is no infection and no drainage is contemplated, the wound is loosely closed with interrupted silk. There is no tension.

Where refrigeration is employed it is unnecessary to place a tape about the vessels, as a tourniquet controls the bleeding

A small series of cases was carried out with this method before the introduction of refrigeration. There were 13 patients operated upon with four deaths, a reduction of the mortality to 33.4 per cent. Still a long way from the ideal!

The problem of anesthesia has been a difficult one, with the aged and infirm type of cases at the City Hospital.

Frederick Allen had worked tirelessly in the experimental laboratory investigating the use of low temperatures as a means of lowering the local metabolic rate to meet the diminished blood supply in the extremities in arterial disease, and, also, he had worked in testing out the anesthetic value of cold. Allen showed that if a tourniquet is applied to a limb of the experimental animal during 54 hours of refrigeration, with a skin temperature of approximately 5°C , the blood does not clot, the vessels do not suffer damage resulting in subsequent thrombosis, and the skin and other tissues remain fresh and intact. Paralysis and other nerve injuries are either prevented or minimized by cold.

The work of Allen was confirmed by Barney Brooks and George Duncan, who showed that rats' tails, rendered completely anemic and refrigerated, could survive more than 96 hours, whereas if the temperature were raised they succumbed much earlier.

Staige Davis showed, a number of years ago, that skin could be preserved in an ice-box for several days and then utilized for skin grafting.

Allen believes that "Refrigeration of tissues has opened up several new avenues for study. Basically, its action is to reduce metabolism to a point which is just compatible with tissue viability. Thus, in a leg with advanced arteriosclerosis, metabolism can be reduced to a level where the existing circulation is adequate for the needs of the tissues. It is possible in embolic blockage to preserve the tissues by cooling for a sufficient period to allow a collateral circulation to develop, and then gradually to increase the temperature as the tissues can tolerate it. Also if amputation becomes necessary it is undertaken through better nourished tissues.

"In the field of anesthesia, refrigeration introduces a fundamentally new concept." According to Allen "It produces an anesthesia of protoplasm instead of a nerve anesthesia." This reduction of temperature produces in the tissues a physiologic blocking of nerve conduction. Along with this, shock is apparently nonexistent, and the low temperature causes a marked inhibition of bacterial growth and enzyme action.

"Animal experimentation, as well as observation in human cases, has shown that cold prevents agglutinating processes such as are seen in the formation of fibrin between the surfaces of a sutured wound. In this way drainage can be maintained in an amputation stump wound as long as is necessary and healing will begin only when the temperature has been allowed to return to normal."

With this experimental background, Allen and Ruggiero, under the stimulation of Lyman Crossman, decided to make the first comprehensive study of

refrigeration on human beings The first operation of this series was performed, July 12, 1941, at the City Hospital A low thigh amputation was performed for arteriosclerotic gangrene

The technic, according to Ruggiero, is as follows "Two turns of a gum-rubber tourniquet (about one-half inch in diameter) is securely placed six or more inches above the level of the skin incision, and above the proposed line of amputation through the bone, completely occluding all the vessels The area which is to receive the tourniquet is previously refrigerated for about ten minutes with cracked ice Then two turns are placed one on top of the other and the tourniquet is fixed with a strong clamp of the type of Kelly or plain Kocher Immediately after the application of the tourniquet the extremity is immersed in a bucket of ice-water and cracked ice, for amputations of the foot and lower leg, for amputations of the thigh, the extremity is packed in finely-cracked ice, with the patient lying in bed The ice is kept in place with a large rubber sheet It is of paramount importance that ice or ice-water extend above the tourniquet for about two inches A low leg operation will require about 25 pounds of ice, a low thigh will require about 50 pounds of ice

"For amputations of the lower leg or foot, immersion for one and one-half hours is sufficient to produce surgical anesthesia lasting up to one hour For amputations through the thigh, immersion for two hours is sufficient

"The patient is brought to the operating room with the extremity in ice He may receive a small preoperative dose of morphine sulphate, but this is usually unnecessary His ordinary eating routine need not be interrupted When the surgical team is ready the patient is placed on the table and his extremity unpacked from the ice The tourniquet is not removed The extremity is prepared in the usual way and the surgeon proceeds with the amputation After the limb is removed and the large vessels are ligated, the tourniquet is removed, and other smaller bleeders are ligated We have utilized the fine silk technic, avoiding undue trauma to tissues It is imperative to use cold instruments, and cold saline solution in the procedure We prefer the Gigli saw to the bone saw About half of the cases we have closed without drains In the face of definite infection the stump was either drained or left wide open

"Postoperatively, the stump is gradually defrigrated, with the use of ice-bags This time of defrigration depends upon the blood supply and the degree of infection present In the presence of good blood supply the ice bags can be removed in 24 hours Infection increases the time of postoperative defrigration

"*Discussion*—With the method outlined, it is possible to secure complete surgical anesthesia for about one hour—sufficient to perform any amputation Primary union of the stump occurs There is no appreciable change in either the pulse or the blood pressure, or of the respirations of the patient during refrigeration, during the operative procedure, or postoperatively Immediately after application of the tourniquet the patient may feel slight pain, but

this disappears within ten or 15 minutes after immersion in the ice. The general diabetic status of the patient is not made worse. It is possible to amputate through definitely infected areas. The mortality and morbidity at the City Hospital using this method has been materially reduced."

Under the combined use of the sleeve-operation, plus refrigeration, the mortality was again halved, so that in a series of 13 amputations there were but two deaths, or a mortality of 15.4 per cent. Both deaths were due to emboli.

CONCLUSIONS

The amputation, as devised by Fuller, with the careful protection of the superficial blood supply at the site of amputation, is well worth emphasizing. If the fascia and skin are not united by clips in the dissection backwards the fascia may be stripped from the overlying fat. We are all aware that the fascia receives its blood supply from the areolar tissue on its surface, and, therefore, every effort should be made in the damaged vascular patient to preserve this relationship. By incising through tendons there is very little shock or postoperative hemorrhage, and by following the femur closely inside the muscle bundles there is very little danger of the spread of infection. Following the amputation the tissues drop together and are sutured without any tension. The artificial leg-maker at the Bronx Veterans' Hospital, which has one of the best orthopedic shops in the country, is confident that the best mid thigh amputation stump is the one that bears weight on the ischium and not on the end of the stump. This bony stump should be at least eight inches long, as measured from the greater trochanter. As the muscles contract, the incision is drawn posteriorly and a very thick muscle pad is left over the femur.

Refrigeration offers a choice of anesthesia in the aged and difficult-risk patient, which is a great advantage. These cases do not show shock when allowed to return to the ward, and they are usually hungry and are fed soon after operation. Pain is relieved by keeping the ice bags about the stump with a small but sufficient bandage over the incision. One might anticipate that thrombi might occur in the long saphenous or femoral vein above the tourniquet during the period of two hours before operation, when the tourniquet is in place. While two of the deaths, noted in this group, were probably embolic in nature, this is an embolic group, and it is hard to state whether this theoretic concept is any factor, until a much larger series has been studied. We have seen cases where there were lymphatic streaks above the knee, which healed *per primam*, so that the application of cold must have some inhibitory effect upon the growth of bacteria in the tissues.

In amputations below the knee it has been possible, with the aid of refrigeration, to be more conservative than has previously been the case. Amputations below the knee have not been discussed in this article because of the limitation of time, but refrigeration and a similar sleeve-operation, beginning just above the ankle, with a longitudinal extension over the fibula, so that the fibula may be excised higher than the tibia, have given very excellent results.

The senior author sees, in the combination of a sleeve-operation and refrigeration, a real advance in the treatment of amputations in the difficult-risk case. Certainly, in our experience, it has done much to reduce the mortality and morbidity in diabetic gangrene amputations above the knee at the City Hospital.

DISCUSSION —DR W F RUGGIERO (New York, N Y) I wish to thank the Association for the privilege of discussing Doctor Bancroft's paper. As in any new method of treatment, there are likely to be some misconceptions, and in this procedure one misconception is that most people think of it as a freezing method. It is not freezing. The temperature of ice is 0°C . It can only solidify water, and the skin and tissues are not plain water, they are primarily colloids and crystalloids in solution, with a freezing point below 0°C . Secondly, the ice is not in direct contact with the skin. It is a film of water at 0°C in contact with the skin, and freezing of skin and tissues, therefore, cannot take place. In one case, after four hours of ice application, the temperature of the skin was 2°C .

Because this new method simplifies the surgery and inhibits infection, one is likely to forget the fundamental surgical principles of handling tissues carefully and meticulously. The silk used is No. 00, and we only use No. 1 silk for the main vessels. We do not use drainage except where there is definite gross infection or areas of pus, then we leave it wide open.

The procedure has several other advantages. If the patient is in poor general condition it is possible to halt the infectious and gangrenous processes and bring him to a better general condition before operating. Occasionally there is bilateral gangrene, and this method makes it possible to perform one amputation at a time, while halting the process in the other leg. It makes possible more conservative and lower amputations without jeopardizing the patient's life. The use of this method in traumatic injuries will help to prevent gas gangrene and various other infections that follow such injuries.

DR MARGARET STANLEY BROWN (New York, N Y) I appreciate very much being given the courtesy of the floor in order to discuss Doctor Bancroft's paper. This work has interested me very much from its beginning. I am quite frank to confess that I was "from Missouri" at first, as I could not see how this treatment could do what they claimed. But after seeing it at first hand, and after carrying out the procedure myself, I am equally frank in saying that I am "sold" on it.

What Doctor David said this morning about the need of adapting treatment to suit the type of patient handled, applies very well here. The City Hospital patients come from the poorest possible social stratum. They are in the upper age-bracket. They live under poor hygiene, their nutrition is very deficient, and the majority have diabetes.

What the treatment does is literally to put them on ice and cool them down until they can be gotten into better condition. With ice bags around the leg, the inflammation subsides and their toxicity diminishes. They can be given fluids and a well-balanced, high vitamin diet. Their diabetic status can be studied.

When ready for operation the refrigeration treatment offers an anesthesia free from shock, which is such a hazard to old people. The condition of the patients on their return to the ward is excellent. Many of them eat a large meal immediately after operation, and enjoy it. Their postoperative course is smooth and, while there are sometimes small areas of slough along the

suture line or in the fascia, there are none of the massive sloughs involving the entire stump

I hope that some of you will have the satisfaction of following some of these cases, and I am sure you will agree that the postoperation expression on their faces tells the story far better than I can

DR CHARLES VENABLE (San Antonio, Texas) In 1924, I reported a series of cases on which a periarterial sympathectomy had been done in the early stage. I made the observation that in diabetic gangrene the patients who had this done improved, and gave us a selection of time for amputation and a healing stump that was better than any I have ever seen, and I have continued since then to do periarterial sympathectomy in these cases

DR BARNEY BROOKS (Nashville, Tenn.) This report of Doctor Bancroft's, as well as those of other observers, concerning the advantage of refrigeration prior to amputation of the extremities, is of great interest to me. I must confess I have some difficulty in understanding how cooling of a part of a body which has been deprived of its circulation by the application of a tourniquet, and which is subsequently to be amputated, should exert any beneficial effect. I believe it is also important to point out that our experiments have shown that refrigeration has a very effective influence on the preservation of the vitality of tissues deprived of circulation, but that although refrigeration prevents the appearance of the usual manifestations of infection, after refrigeration is discontinued, there is definite evidence that the destructive effects of infection may actually be increased

DR FREDERIC W BANCROFT (New York, N Y, closing) Refrigeration provides an anesthetic which is accompanied by very little shock. Many of our patients were in the 70 and 80 age-group, and they were the neglected type of case. They show very little shock at operation, and on being returned to the ward are allowed to eat. If ice bags are employed over the dressing for three or four days postoperative, we have not noticed necrosis. There has been some delay in healing, and it is advisable not to remove the sutures before the twelfth day. Some of these patients do have some tissue sloughing, but I have not been able to feel that it has anything to do with refrigeration. It may be wise to suggest that the preoperative therapy is not actual freezing, as the temperatures taken by skin thermometers show them to be about 5-10° C. Where there is chopped ice there are air spaces which prevent the temperature from getting too low

INTERINNOMINO-ABDOMINAL (HINDQUARTER) AMPUTATION*

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SINCE Gordon-Taylor and Wiles's⁵ complete study on interinnomino-abdominal amputation, new interest has been aroused in this therapeutic procedure. Most surgeons have encountered pathologic conditions involving the innominate bones or upper portions of the thigh and adjacent pelvis for which therapy has been inadequate. No surgeon, except Gordon-Taylor, has had any experience of consequence in the undertaking of this formidable type of surgery. Nevertheless, there are times when such heroic measures offer the only possibility, at present, for the relief or for the eradication of an otherwise impossible situation.

In a subsequent report five years later, Gordon-Taylor⁶ stated that he had performed the operation six times during the intervening period bringing his experience to 11 cases. He mentioned that W. H. Ogilvie, Harry Platt, Duncan Fitzwilliams and Grey Turner, among English surgeons, also had employed this operation successfully—some of them more than once, and that Harris, of Toronto, and McCaw, of Auckland, had done it as well. I could not find reports in the literature by these surgeons except in the case of Fitzwilliams.³ Consequently, as Gordon-Taylor himself gave no references in regard to these operations, I assume that this statement was made from personal communications by them to him.

The literature from 1935 to date reveals that in addition to the six new cases of Gordon-Taylor⁶ there have been possibly 12 others reported.

Brief accounts of these cases are as follows:

Banet and Noho.¹ Male, age 27. Fibrosarcoma of lower end of left femur. One transfusion. Anesthesia not stated. Operation—shock. Transfusion. Radiation therapy 1,000 r units. Outcome not stated.

Fitzgerald.² Male, age 13. Osteogenic sarcoma of right hip. Spinal anesthesia. One transfusion. Out of the hospital walking on crutches in 22 days. No late report.

Fitzwilliams.³ Male, age 62. Rhabdomyosarcoma of vastus internus, with extension to gluteal region. Three transfusions. Good recovery. Up and about, oldest recorded patient to undergo this operation. No late report.

Gersh.⁴ Male, age 60. Sarcoma upper epiphysis and neck of femur. Spinal anesthesia. Good recovery. Wound infected, extensive erysipelas. Two months severe hemorrhage from wound. After one month, death from cachexia. Postmortem. Recurrence deep in wound, sacroiliac joint, symphysis pubis, peritoneum. Hemorrhage from newly formed vessels in tumor.

Leriche and Stulz.⁷ Male, age 33. Chondromyxoma of left thigh with extension to pelvis. Ether plus procaine to nerves. Good recovery. Some of flap sloughed grafted, up on crutches in two and one half months, not quite healed.

Leriche and Stulz.⁸ Male, age 29. Ewing's sarcoma diffuse left femur with spontaneous fracture. Ether, plus procaine infiltration. Good recovery. Healed and walking with crutches in three weeks.

Padovani.⁹ Male, age 18. Enormous tumor right pelvis—mameloma. Ether, plus procaine to

* Read before the Southern Surgical Association, Pinchurst, N. C., December 9-11,

nerves Two transfusions Normal healing General condition not improving since operation, anemia, etc

Pascalis 10 Male, age 44 Osteosarcoma left iliac region Spinal anesthesia and ether Transfusion Patient died

Rapant 11 Male, age 29 Recurrent osteogenic sarcoma upper third of left femur Two transfusions then spinal percarne anesthesia Patient gained weight postoperatively but metastasis occurred in right iliac bone

Rapant 11 Male, age 14 Osteogenic sarcoma of the left femur Ether anesthesia Collapse Intravenous therapy Transfusion next day Two weeks later was healed

Ricard and Clavel 12 Male, age 36 Malignant tumor of upper end of femur Bad shape Repeated transfusions before operation General anesthesia Transfusion Good day following operation but died in following night, suddenly

Shvarts 13 Male, age 48 Periosteal sarcoma of the left hip Ether anesthesia Transfusion during operation Drainage Patient died 27 days postoperative from reactivation of an old tuberculous pulmonary lesion and septicemia The latter was due to necrosis at the seat of operation



FIG 1—Case 1 Destructive lesion about hip joint with soft tissue mass laterally and medially

I should like to record four causes in which interinnomino-abdominal amputation was performed at the Strong Memorial and Rochester Municipal Hospitals

CASE REPORTS

Case 1—Hosp No 43193 I D, female, age 51, was admitted to the Strong Memorial Hospital, November 2, 1939 For two years or more she had had mild pain in the right hip This caused her to limp Gradually the pain became more intense, radiating up and down the leg especially to the region of the knee joint Several physicians treated her without benefit The limp by this time was pronounced The pain had also

increased to such an extent that she was sent to the County Hospital in February, 1939. Because roentgenograms were suggestive of tuberculosis, she was transferred to Iola, where she remained for five months. A plaster spica relieved her of pain, but after four months in it the disease showed no evidence of improvement. A needle biopsy confirmed the diagnosis of a malignant tumor. She had stabbing pains in her right thigh whenever the right hip was moved. Otherwise she remained free of discomfort.

Examination showed a rugged woman, with pallor. There was a mass palpable in the right lower quadrant. The right hip was moved guardedly. There was very little joint motion present. There was apparent shortening of one inch. The limb was held in complete extension, with about 15° of external rotation. There was evidence of muscular atrophy of the whole limb. A firm, palpable, tender mass could be made out between the iliac crest and the great trochanter. This swelling seemed to connect with the mass in the right lower quadrant. The right inguinal nodes were firm, enlarged and quite tender.

Her vital signs were normal. Laboratory examinations showed normal red and white blood cells and hemoglobin. The urine had a trace of albumin but no sugar. Roentgenograms gave evidence of an extensive destructive lesion about the acetabular region, incomplete outline of the femoral head, and a large soft tissue mass laterally, above the femur, and medially encroaching upon the pelvic cavity (Fig 1).

She was given a thorough course of roentgenotherapy to the hip during the course of the next month. She received 40 treatments of 300 r units, for a total of 12,000 r. Her pain was lessened somewhat but there was no appreciable effect on the tumor. Surgery was advised at this time but she wanted time to think it over. She remained at home for one month, staying in bed and suffering severe pain on any motion of the hip. The tumor had made some growth progress during this time but there were still no signs of lung metastases.

On January 9, 1940 a right interinnomino-abdominal (hindquarter) amputation was performed. She had acute retention requiring catheterization for two days postoperatively. There was moderate distention which was relieved by a Wangenstein suction tube. She ran a moderate febrile course during the next ten days. On the eleventh day she drained foul pus into the vault of the vagina. There had been an abscess in the prevesical space from which *E coli* and anaerobic streptococci were cultured. This cavity was drained adequately by making an incision above and introducing through-and-through drains. The temperature returned to normal following this treatment. The infection was gradually brought under control and the sinus closed in. Her bowels were kept constipated by opium pills till the sixth day postoperatively. After that time there were almost daily controlled movements, without difficulty. She began to walk with the aid of crutches after the fiftieth day. She was discharged from the hospital in excellent spirits, without any complaints, two months after entry.

Pathologic Examination—Gross The specimen showed a tumor mass measuring 18x12x10 cm. It was boggy and gelatinous in consistency. It surrounded the upper ramus of the pubic bone, arising from a broad base over the obturator foramen. The bone was fractured in this area. The tumor was egg-shaped, well encapsulated, and had an anterior globular extension, about 8 cm in diameter, over the hip joint. Gelatinous tumor tissue was found within the joint capsule. The capsule of the tumor had been broken in one small area near the medial side (Fig 2).

Microscopic examination showed cartilage as the predominating cell type, though there was an abundance of myxomatous tissue as well. Spindle-shaped cells were scattered throughout the tumor. Frequent mitoses were observed. Tumor tissue was seen within the lumen of a blood vessel in one section. *Pathologic Diagnosis* Osteogenic sarcoma, chondro-type (Fig 3).

She was readmitted to the hospital, December 10, 1940, because she had lost weight, had increased thirst, and frequency of urination. She began to have pain referred to her



FIG 2—Case 1 Gross specimen Osteogenic sarcoma—chondro type

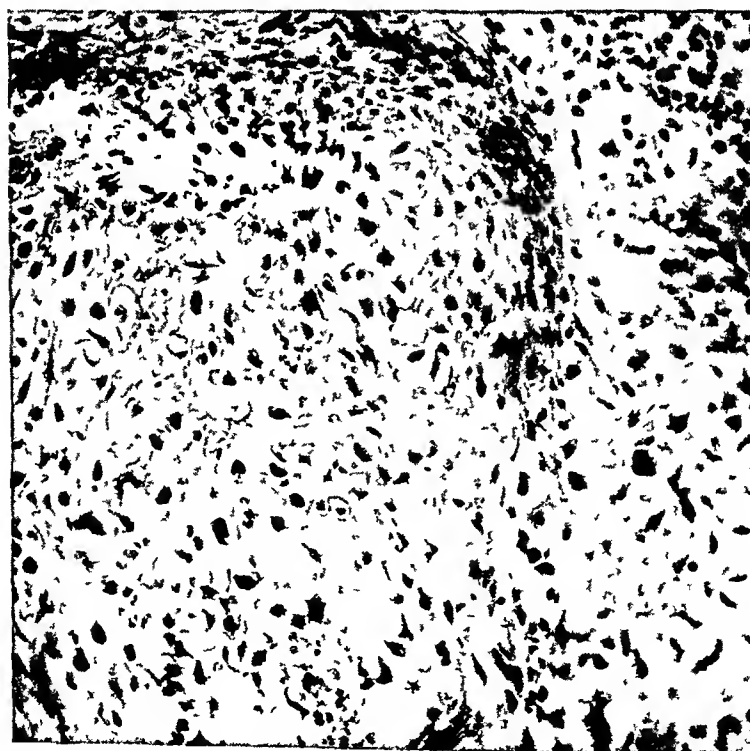


FIG 3—Case 1 Microscopic section Osteogenic sarcoma—
chondro type (X210)

amputated leg shortly after leaving the hospital. This had increased in severity. There was also a small sinus present on the stump.

Upon examination, she was found to have diabetes. This was brought under control with insulin. The sinus tract was excised under pentothal sodium anesthesia. Two pieces of silk which had been used to ligate the external iliac artery formed the basis for the sinus. Roentgenograms of the lungs showed areas which were suspicious of a pneumonic process. She was discharged in good condition, December 29, 1940.

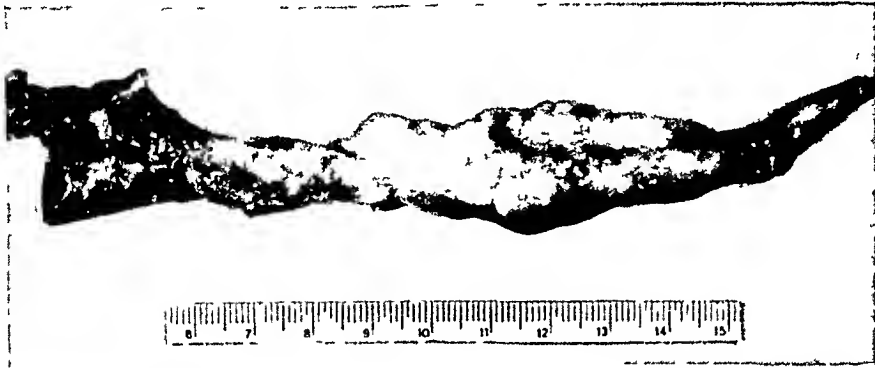


FIG 4—Thrombus of tumor tissue found in the right iliac vein at postmortem examination

She continued to have pain referred to the amputated leg and knee. On January 6, 1941, she felt weak, drowsy, and listless. She had been receiving morphine pills every 3-4 hours for pain. She had a cough with no sputum production. There were many rales at both bases, more on the left than on the right. A diagnosis of metastases to the



FIGS 5 and 6—Roentgenograms taken in 1935 and 1940 showing the progressive growth and extension into the soft parts

lungs was made. The patient was sent to the County Hospital. She was kept comfortable there, with sedation as necessary. She died February 4, 1941.

Autopsy—The tumor had recurred in the right pelvic region. There was invasion of the sacrum and the muscles of this area. A tumor thrombus occluded the right iliac vein, with extension into the inferior vena cava (Fig 4). Tumor thrombi were found in both pulmonary arteries. Numerous metastases were present in the lungs, bronchial lymph nodes, liver, spleen and left kidney. There were multiple infarcts in the left kidney, with tumor thrombi in the renal arteries. There was an old organizing pneumonia.

It was of interest that one of her sisters died of "carcinoma of the liver" and a brother has diabetes at the present time

Case 2—Hosp No 161737 M M, white, male, age 54, was admitted to the Rochester Municipal Hospital, February 1, 1940. He had had rather severe pain in his left hip for the past eight years. He was admitted to the Genesee Hospital, Rochester, N Y, four years ago. A tumor was exposed and curetted away from the region of the greater trochanter. It was thought to be a slow-growing osteochondroma from the microscopic examination. Some doubt must have remained in the mind of the clinician for hip joint amputation was advised and refused. Following this, a course of roentgenotherapy was administered at the State Institute for Malignant Disease. There was a gradual recurrence of the tumor, with diffuse enlargement of the left hip region. Stiffness of the joint and pain on weight-bearing became annoying features. The pain was almost constant, kept him awake at night, and required opiates for relief. He received an injection of 1 cc. of 95 per cent alcohol into the second lumbar spinal canal at the State Institute for Malignant Disease, August 15, 1939. Some relief was obtained, but it was transient. Other sequelae of this treatment were weakness of the left leg, numbness and tingling of the left foot, and a constant sensation of coldness in the left leg. He also had difficulty in starting bowel movements and urination. At the date of entry, there was considerable iliosacral pain on sitting, lying, or standing. He had to get out of bed three to four times a night to get relief.

Examination showed an obese man, with the left hip held in 45° fixed flexion. There was a firm, bony-hard, globoid mass involving the whole upper end of the left thigh. It was an enormous tumor with ill-defined margins. It infiltrated the gluteal muscles posteriorly. Apparently, the pelvis was invaded by it. The upper half of the thigh was tense and tender. There was a long curvilinear scar over the lateral surface of the growth. A sinus, with swollen, reddened edges, discharged thin, serous material. Any attempted motion of the hip was accompanied by pain. The muscles of this limb had poor tone and there was very little muscular power left. Marked atrophy was apparent in the leg muscles. Examination otherwise was essentially normal.

Laboratory studies showed a mild secondary anemia. The blood total proteins were normal. The Wassermann reaction was negative. Culture from the sinus grew *B. subtilis*. Roentgenograms revealed a soft tissue mass over the trochanteric region completely surrounding the bone. The cortical line of the bone had been destroyed from the hip articulation down to the midshaft. Irregular cotton-wool density was present externally to the shaft. Bone destruction and irregular bone production were evidences of an osteogenic sarcoma, chondro-type (Figs 5 and 6). Roentgenograms of the chest showed no evidence of metastasis.

A modified hindquarter amputation was performed, February 7, 1940. The modification was necessitated by the fact that the gluteal muscles had to be sacrificed because they were infiltrated by tumor. Accordingly, an attempt was made to preserve the skin over the adductor muscles together with the obturator artery as blood supply so that this block of tissue could be rotated upward to cover the stump. The adductor muscles did not appear well vascularized at the close of the operation so they were removed. The operation was well borne. The skin looked pallid but there was no tension on it. Although its survival was questionable, it was left in place for the time being. The upper part appeared necrotic and was removed five days later. Most of the rest of the skin also came away during the next week. Dakin's solution was applied to the wound, alternating with normal saline. Clean granulations resulted. Split thick grafts and pinch grafts were used to cover in the granulating area. Epithelization gradually took place. He began to walk with crutches, progressing quite nicely before his discharge from the hospital 60 days after admission.

He was put on constant bladder drainage immediately after operation. This was discontinued after one week. Bladder function appeared to be normal while in the hos-

pital. But three weeks after discharge he had difficulty in voiding, frequency, urgency, and terminal dysuria. Urine culture showed *E coli*, and *Staphylococcus albus hemolyticus*. There was no residual urine. There was an anterior stricture found which was dilated up to a No 24 F sound. This gave him complete relief from his urinary complaints.

No attempt was made to regulate the bowels. He did not have a movement until one week after operation. After that the function appeared to be regular without necessity of any medication.

Pathologic Examination—Gross The specimen consisted of a huge, rather diffuse tumor, involving the upper end of the femur, particularly the lateral aspect. There was a dirty, 15 cm, ulcerated area in the region of the greater trochanter. This was the

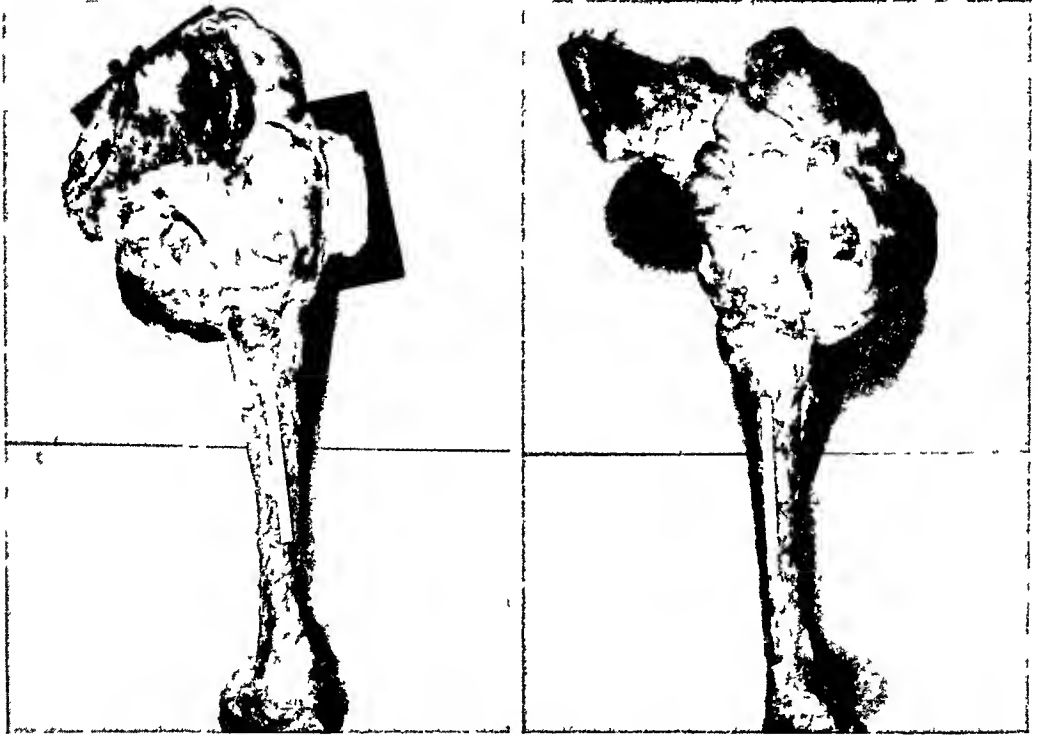


FIG 7—Case 2 Gross specimen Osteogenic sarcoma—chondro type

sinus from the previous operation. The tumor was exposed after dissecting away the psoas and gluteal muscles. It was encapsulated, boggy, dull gray in color, and measured about 25 cm in diameter. The tumor was lobulated, and upon section into the capsule grayish-pink, jelly-like material was released. The tumor tissue had extended laterally into the old operative area. The hip joint was buried in the mass which involved the entire upper fourth of the femur, and was in contact with the pelvic bones above. There were three smaller tumor masses, up to 3 cm in diameter, along the posterior surface of the femur below the main tumor (Fig 7).

Microscopic sections showed an intact connective tissue capsule. Some portions of the tumor were entirely myxomatous in appearance. Usually, in this myxomatous stroma there were several types of cartilage cells. The most common type had a pale pink nucleus surrounded by a clear halo and then a dark membrane. Similar nuclei were larger and vacuolated. Scattered smaller cells with dark staining nuclei were present. Occasional mitotic figures were encountered. Very pale young cartilage was observed in some areas (Fig 8).

He was practically asymptomatic until a recurrent tumor was noted in the stump. This was accompanied by some local pain. There had been some sensation of pain

referred to the absent limb at times. He had gained weight. He got around on crutches quite well. The recurrent tumor measured 8x10 cm of indurated tissue, intermingled with the old skin grafts. The whole skin-grafted area was excised, and with it a mushy, gelatinous tumor, about the size of a grapefruit, which extended down to the bone. It ruptured in several places during removal, but the area was thoroughly washed with saline solution and left open to granulate. Pathologically it showed chondrosarcoma with myxomatous change (Fig 9). A split thickness graft was sutured over the granu-

FIG 8

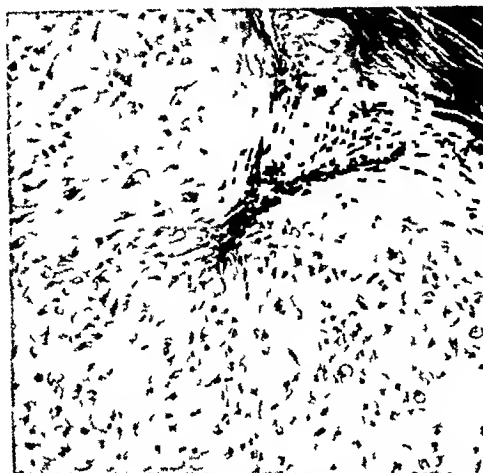


FIG 9

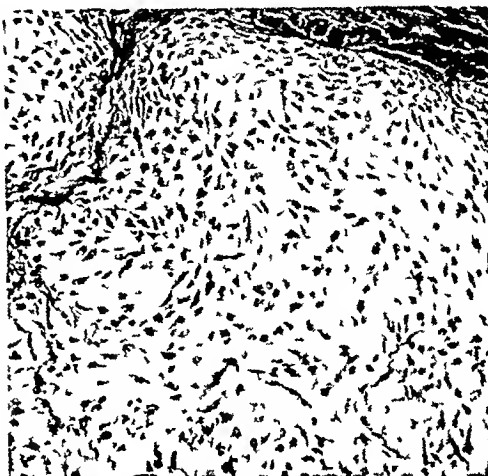


FIG 10

FIG 8—Case 2. Microscopic section from original resected tumor ($\times 210$)

FIG 9—Case 2. Microscopic section from recurrent tumor in stump, more aggressive and myxomatous

FIG 10—Case 2. Microscopic section from metastatic tumor in rib. Typical osteogenic sarcoma, with no cartilaginous elements

lating surface and it healed nicely. The first of these operations was on August 25, 1940, and the second on October 5, 1940.

His next admission to the hospital was December 4, 1940. For about three weeks there has been steady aching along the lower left costal margin and in the back. A lump was found on examination over the tenth rib in the midaxillary line. It was excised *en bloc*, with portions of the adjacent ribs, nitrous oxide-oxygen-ether anesthesia being used. He was discharged December 22, 1940.

The microscopic examination showed this tumor to be absolutely unlike the previous cartilaginous types. It had the characteristics of an osteogenic sarcoma (Fig 10).

Subsequent Course—January 14, 1941. He still complained of chest pain and also pain referred to the absent leg. In other respects he appeared to be getting along fairly well.

He developed progressive swelling of the left eye, with dull pain, after leaving the



FIG 11—Case 3 Area of destruction in acetabular region



FIG 12—Case 3 Central dislocation of head of femur through tumor of acetabular region

hospital There was diplopia on looking to the left In the Spring, examination showed left exophthalmos, limited ocular motility and increased intra-ocular tension There was also pain in the back and over the left eye Relief was obtained by drugs Roentgenotherapy was administered over the painful areas, with a satisfactory result It was apparent that the metastases were wide-spread by this time He died October 3, 1941 Postmortem examination was not secured

Case 3—Hosp No 162734 A S, white, female, age 42, was admitted to the Strong Memorial Hospital February 29, 1940 She had complained of pain in the right hip for about one year Two months before this time she had had a fall The pain was most severe on weight-bearing She walked with a limp in consequence Any rotation of the hip joint caused discomfort

She appeared to be in acute distress She was obese and cooperative Her thyroid gland was two to three times the normal in size and had the smooth, nodular areas characteristic of benign adenomata There was a soft systolic murmur over the mitral area There was tenderness on deep palpation over the right hip Hip flexion was restricted 20° as compared to the other side, also external rotation and abduction were not within 40° of the normal motion of the left hip She had no evidence of an infectious process Careful survey for a primary malignant growth revealed nothing definite

Laboratory studies were all within normal limits Roentgenograms showed degenerative changes in the lumbar spine Stereoscopic roentgenograms of the right hip indicated a large, destructive lesion of the right iliac and ischial bones (Fig 11) Chest films were negative for metastases

Sufficient biopsy material was not obtained by aspiration of a deeply-seated, pulsating tumor, which could not be adequately exposed She was given a course of roentgenotherapy, consisting of 3,800 r units to the right hip, from April 11, to May 2, 1940 On April 18, a small nodule was removed from the neck on a suspicion of malignancy It proved to be a sebaceous cyst She was discharged, May 2, 1940, without much sign of improvement Her diagnosis was uncertain, but a presumption that it might be a primary giant cell tumor of the right ilium and ischium was entertained

She was given an additional 1,000 r units of roentgenotherapy during the following week, completing a cycle of 4,800 r units to the right hip

On May 26, she fell, striking on her left hip There was immediate pain in the right hip She was unable to walk Pain was severe Motion of the hip increased the pain Aching continued in the right hip region without abatement She was readmitted to the Strong Memorial Hospital June 8, 1940 She appeared to be haggard with pain and long-suffering Both legs were propped up on pillows, the knees and hips in partial flexion There was apparent shortening of one inch of the right leg, which was held in 20° of internal rotation and adduction The right hip was fixed and painful Roentgenograms showed a pathologic fracture through the right acetabulum, with central dislocation of the head of the femur (Fig 12) Films of the chest gave evidence of a mass in the anterior mediastinum, displacing the trachea—either a substernal thyroid or perhaps a metastasis There did not seem to be any alternative to a hindquarter amputation This was, accordingly, carried out, June 11, 1940 The operation was difficult, and some shock resulted Transfusion restored her pressure to normal at the close of the procedure The gluteal muscles were preserved to cover the denuded area which was closed without tension

The postoperative period was relatively uncomplicated She voided spontaneously, and the bowels moved without medication on the third day The wound healed without incident She was out of bed in two weeks Within one month she had learned to use crutches satisfactorily She had pain referred to the amputated limb for about ten days

The specimen showed a pathologic fracture across the acetabulum, with the femur head projecting through a soft, yellowish-gray tissue (Fig 13) Microscopic sections were typical of metastatic carcinoma from the thyroid (Fig 14)

The thyroid gland was subjected to reexamination by a number of surgeons, and

none of them would have made a diagnosis of malignancy from its consistency. She was given a course of roentgenotherapy over the gland—3,900 r units in about a month. She has been followed in Tumor Clinic since operation. On December 26, 1940, her general condition was good. There was an occasional slight discomfort in the operative

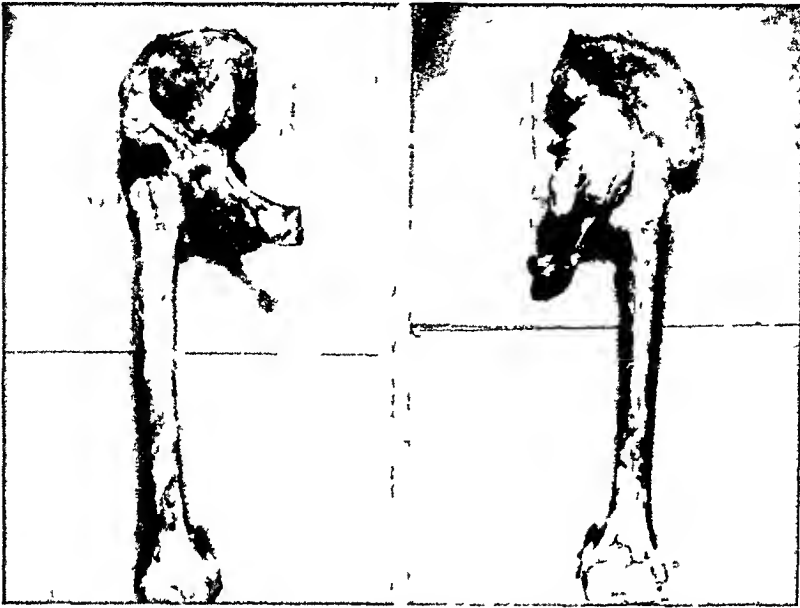


FIG 13—Case 3. Gross specimen. Metastatic thyroid tumor with fracture of acetabulum and central dislocation of head of femur.



FIG 14—Case 3. Microscopic section. Metastatic thyroid carcinoma (×210).

area. No definite evidence of recurrence or additional metastases were noted. The thyroid showed little change.

November 6, 1941. The patient showed a gain of ten pounds over her original weight on her first admission. There were no evidences of recurrence nor metastasis elsewhere. The thyroid remained unchanged. She has had amenorrhea for four months, probably

on a menopause basis. The pelvic examination revealed nothing significant. Occasionally she has twinges of pain in her absent limb (Fig 15).

Case 4—Hosp No 166848 C J, male, age 55, was admitted to the Strong Memorial Hospital June 26, 1940. He was an intelligent man who had had an interesting career in spite of chronic invalidism which dated from his eighth year. A fall had caused a fracture of the left arm, with bruising of the left hip, in 1892. During the following year there were sharp pains, involuntary contraction of the hip and knee muscles, and failure of the left limb to grow as rapidly as the right. In 1894, a large abscess had formed about the left hip joint. It was opened and pieces of necrotic bone were excised from the head of the femur and the acetabulum. He was in bed for seven months, on pulley weight-traction, in Burlington, Vt. In 1895, an extension steel brace



FIG 15—Case 3 End result

was worn, but, in spite of this, another abscess formed and was drained. Some iodoform compound was used to irrigate and pack the wound. From 1896 to 1905 there were repeated closures and incisions for abscesses and curettage of dead bone. In 1906 the bone was curetted twice. While a student at Harvard, from 1907 to 1909, there were similar episodes. He spent most of the summer of 1909 in a complete body encasement at Cambridge, Mass. Dead bone was removed on several occasions in New York City between 1910–1914. Roentgenotherapy was tried experimentally, in the latter part of 1914, to see if the condition could be improved. He was curetted for necrotic bone on an average of once a year from 1915–1920. Carrell-Dakin treatment was employed during this period. A heavy compound of wax and bismuth was forced into a dead space in the left groin to promote healing, about 1920. Frequent abscesses formed and dead bone was removed during the next seven years. In 1928, a large piece of necrotic bone was excised from the head of the femur. By 1932, the femur head had completely disappeared, and the socket had been cut or sloughed away. An attempt to induce an ankylosis of the hip area was made in Syracuse, New York. He was in a body encasement for several months. He wore a light celluloid encasement during the rest of the year. The fusion failed, however. The following four years were associated with abscess formation and beginning intense pain. Surgeons tried to remove as much scar tissue as possible, because it was thought to be causing the nerve pain by pressure. Strenuous Swedish massage was employed also to loosen up the scar tissue. As a result of this latter treatment another series of abscesses developed. These were opened during

1936-1938 Treatment with the Kromeyer ultraviolet light, water-cooled tube, was employed, but apparently without effect In 1938, another attempt at fusion of femur to pelvis was carried out unsuccessfully Bacteriophage was introduced through the summer of 1939, also "permase," "allantoin," and "urea" The pain continued to be intense Some days it was difficult to walk on crutches at all He obtained little sleep Often, he was more tired on arising in the morning than he was when he went to bed the night before He had discomfort at times in the area where the bismuth-wax was injected Pain also centered about the closed sinuses on the buttocks near the back There were shooting pains on the inner side of the thigh between the groin and knee He summarized his operations as follows Between 1892 and 1940 there had been 39 major operations and curettings He estimated that, in addition, there had been about 20



FIG 16—Case 4 Roentgenogram indicating chronic osteomyelitis of left ilium, loss of femur head, and bismuth paste previously injected

minor incisions with drainage By May, 1940, he had reached a point where the continuous pain had become unbearable His attending physicians had made conscientious trials to give him relief by every possible means short of morphine, but finally had to resort to this drug In consequence, he had been taking $\frac{1}{2}$ to $\frac{3}{4}$ gr of morphine daily, for his torturing pain In June, 1940, he wrote "Frankly, this is with me a life and death emergency I cannot work and earn until this pain is conquered"

Examination showed him to be a small, poorly-developed and poorly-nourished man There were numerous coarse râles throughout both upper lung fields, which persisted following coughing There was a large, left indirect inguinal hernia The left leg exhibited a retarded development, marked atrophy, and decrease of active motion The left hip joint showed abnormal mobility, but with limitation in flexion The left limb was greatly shortened and deformed It was useless as far as weight-bearing was concerned There was an acute infection present Thick pus was draining from a sinus, posterior to the left hip joint region A considerable amount of pus could be obtained by pressure over this region, indicating a pocket of some dimensions Culture showed *Staphylococcus aureus hemolyticus* present The temperature ranged to 100° F daily The white blood count remained at 12,000 during the first week

Roentgenograms revealed marked atrophy and lack of development of the left innominate bone The bone had many spotted areas of decreased density scattered

throughout. The head and neck of the left femur were missing, the thinned-out, frail-looking shaft resting against the remnants of the outer shelf of the acetabulum. Two foci of increased density were noted, one centrally, over the ilium proper, and a second in contact with the acetabulum. These areas indicated the injection sites of the bismuth formerly used in treatment (Fig. 16).

It was decided to remove the involved innominate bone. After treating him for ten days, in the hope that the infection would clear up, it was apparent that nothing was being accomplished. The sinus continued to drain freely and the temperature stayed about the same. Accordingly, July 6, 1940, a hindquarter amputation was carried out. Care was taken to avoid the draining area as much as possible but, during the procedure, pus was encountered in several different areas. The external iliac artery was distorted

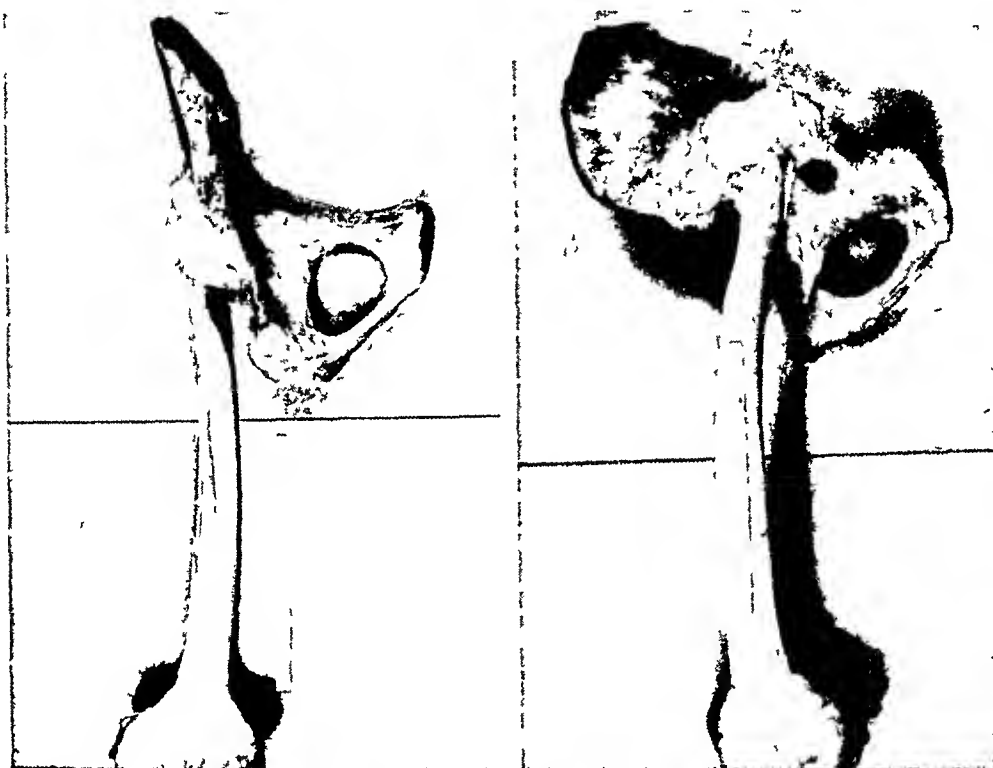


FIG. 17—Case 4. Gross specimen. Chronic osteomyelitis, left innominate bone.

by adhesions from the injection with bismuth paste. The difficulty was overcome by careful dissection. The sciatic nerve was tied with catgut ligatures, and 95 per cent alcohol was injected between the ligatures. Closure was not attempted except to cover the sciatic area. A small portion of the ilium overlapping the sacrum was left in place. The wound was packed with vaselined gauze after carefully irrigating it with normal saline solution.

Shock was combated by transfusion at the close of operation. He was placed on tidal drainage immediately after return from the operating room. He did surprisingly well. He was sitting, well propped up in bed, reading on the day following operation. He was taken off tidal drainage two days after operation. There was no further trouble with his bladder. His bowels moved spontaneously on the fifth postoperative day. The function became normal, daily, by the tenth day after operation.

The wound was infected after operation but it was in condition to skin-graft it after 19 days. The lower limb of the amputated specimen had been saved by disarticulating it at the knee joint and keeping it in an ice-box at approximately 34° F. Split-thickness grafts were taken from this source and sutured over the granulating area with horsehair. Pressure dressing with a sea sponge was applied. One area failed to take but the rest of the grafts took well and spread rapidly.

His major problem was that of morphine addiction. Attempts were made to break this habit by substitution of other hypnotics. This was only partially successful. Intravenous snake venom was used in 1 cc dosage on several occasions. Insulin treatment was also employed. During the last three weeks of his hospital stay he received only one dose of morphine. He was dissatisfied with his sedative orders, complained of severe pains in the absent limb, and frequently asked for morphine. It was certain that he would resume the habit as soon as he could be supplied with the drug. He was discharged, with two-thirds of his wound well healed about two months after admission, August 28, 1940. He had been up and about on crutches for one month prior to discharge.

By the middle of November, 1940, he had completely healed over. He still complained of pains referred to his missing limb. No medication completely relieved him, according to his letters. He spent many sleepless nights. In January, 1941, he had resumed his morphine because of unbearable pains in the missing foot. The operation had apparently accomplished little except the removal of a chronic recurring, draining osteomyelitic focus (Fig 17).

He was readmitted to the hospital, February 11, 1941. Since going home he had shown general improvement. He had been up and about most of the time on crutches. But he had severe pain in the amputated stump. It consisted of a tight constriction in the knee, foot, and toes of the amputated limb. He required $\frac{1}{2}$ gr of morphine every four hours for relief of this. Examination gave no information of value. Psychologic examination indicated some deterioration from an originally high intelligence level. The psychiatrists felt that he was well adjusted, that he showed no evidence of mental disease, and that the morphine addiction was very mild. On February 28, 1941, a bilateral prefrontal lobotomy was carried out under procaine anesthesia. When the frontothalamic tracts were cut, he declared that the pain in his leg had disappeared. He remained confused and subdued for several days postoperatively. At the time of discharge from the hospital, March 28, 1941, he was caring for himself without assistance. He stated that he still had pain in his absent leg but he did not enlarge on it for 20 minutes as he would previous to operation. He had received no drug of any kind since operation. What the ultimate outcome will be is an open question. A letter from his wife, October 16, 1941, states that he has had no morphine nor other opiate since operation. He has been irritable, abusive and ill-tempered at times. He has returned to work in a minor capacity.

Discussion—All writers on this subject stress two points (1) The necessity for careful hemostasis, and (2) the avoidance of surgical shock. There can be no disagreement on these points. Every surgeon should strive for these ideals in every operation. It is only in the means employed to attain these ends that opinions may differ.

Many surgeons are of the opinion that shock can be prevented by blocking nerve channels and thus keeping harmful stimuli from acting. Consequently, spinal anesthesia is advocated, also, careful exposure and local anesthesia to every nerve trunk, especially the larger nerve cords, such as the sciatic. Leriche even advocates interstitial local infiltration of all the tissues. Personally, I do not believe that this makes very much difference.

In none of our cases was spinal anesthesia employed. In no instance were any of the nerves blocked by procaine infiltration. Division of the sciatic by the cold-knife, or by electrocoagulation with the radio-knife was not followed by any appreciable blood pressure change. The blood pressure readings were carefully recorded every ten minutes throughout the operation.

Neither did injection of the severed sciatic nerve stumps with 95 per cent alcohol cause any reaction

Far more important in causing shock is rough handling of tissues. In our clinic, care and delicacy of manipulation follow the trail blazed by Kocher, Halsted and Cushing, whose contributions in this direction have been too little appreciated

Consequently, time is of minor importance, especially if the anesthesia is well administered. We feel that less harm results from a deliberate, gentle three-hour operation than by a slashing exhibition of unnecessary speed, with inevitable damage to the tissues. Loss of blood cells and, more important, loss of blood plasma are determining factors in shock. If the circulating blood volume is greatly reduced, the cardiac output, per minute, also will be restricted. The blood pressure will drop, vasoconstriction of the periphery will follow, and surgical shock will result. Measures to save as much of the blood volume as possible should be instituted. Consequently, the external iliac artery should be tied before the vein, and the limb elevated to drain as much of the circulating blood as possible from the part about to be removed. It would be well if this limb could be kept higher than the heart level throughout operation, because there must be approximately one-sixth of the circulatory volume in this large portion of the anatomy. It has been our policy to start a slow intravenous infusion before beginning operation. During the operation as much as 1,000 cc of 5 per cent glucose, in Ringer's solution, has been administered. If the patient begins to show shock, whole blood transfusions can be carried out through the same apparatus. In our four cases, Case 2 showed no shock, Case 4, relatively little shock, though the blood pressure dropped until transfusion restored it, Case 1 had some shock which required treatment by two transfusions of 600 cc each. She left the operating room in good condition, with a blood pressure of 100/70 following this treatment. Case 3 had rather severe shock due to two complicating factors—(1) severe trauma of injury, and (2) heavy previous radiation. Consequently, at operation there was considerable blood loss. Two transfusions of 700 cc restored the blood volume and the patient left the operating room in good condition.

In regard to anesthesia, the surgeons have no general agreement. Many favor spinal anesthesia. This would be a good choice for the more rapid type of operation. But Gordon-Taylor emphasized the necessity of extreme care, especially, when changing the patient's position, as is necessary in this operation. Continuous spinal anesthesia, as now practiced, has not been employed, but might be to advantage. General anesthesia with local block to the nerve trunks has had its advocates. In our cases avertin with nitrous oxide-oxygen-ether sequence was employed in Cases 1 and 4. Sometimes, the avertin depresses the blood pressure at the start. Consequently, only a small quantity would seem advisable, merely as a basal anesthetic. In Case 2, vinethene induction followed by drop ether was satisfactory. In Case 3, simple nitrous oxide-oxygen-ether sequence was employed.

As to the position of the patient on the table, it is best to start with the patient flat on his back. The anterior part of the incision then is made from the symphysis along the iliac crest to the posterior superior spine. The anterior dissection is developed extraperitoneally. The external iliac artery and vein are transfixed by sutures and divided. The division of Poupart's ligament makes for easy access to these vessels. The rectus abdominis is freed and the symphysis divided. The patient is turned on the sound side and the incision carried posteriorly down to the gluteal fold and across the trochanteric region to the inner side of the thigh. The perineal incision joins the inner end of the anterior incision over the symphysis. The iliac bone is divided from the crest to the sacrosciatic notch. Saw, chisel, or bone cutters may be employed for this. The gluteus maximus may be saved in most cases, unless involved by tumor. It is well to preserve its blood supply if possible. The iliopsoas muscle is divided, the piriformis and levator ani also. The sciatic nerve cords now lie exposed. Division of these huge nerve trunks frees the limb and leaves a gaping wound. The peritoneum and transversalis fascia remain as the sole protection for the peritoneal contents. The small portion of ilium remaining attached to the sacroiliac joint may be removed or left, as indicated. We have found that the orthopedic trough used for hip joint amputation facilitates the handling of the patient and makes the manipulation toward the sound side easily carried out.

While much has been written regarding the type of skin flaps to cover the stump, it would seem that the decision must rest with the type of diseased involvement of the limb. When it is possible to save the gluteus maximus and a sufficient part of its blood supply, it makes a very satisfactory covering. This was possible in Cases 1 and 3. Leriche, in the first of his articles, advocated ligation of the common iliac artery for control of bleeding. But this was followed by necrosis of the gluteal muscle and delayed healing. The majority of surgeons now ligate the external iliac artery only. When tumor tissue has extended into the gluteal muscles, flaps must be developed in other situations. In Case 2, a long flap, supplied by the obturator artery, was raised to cover in the stump. The blood supply proved inadequate and the skin sloughed, necessitating a skin-grafting operation when granulations had appeared. In Case 4, the limb was grossly infected. Thick pus was expressed from the sinuses during operation. A guillotine-type of amputation was, accordingly, performed. No attempt was made to cover the denuded area. In spite of the fact that only the peritoneum and the transversalis fascia remained between the abdominal contents and the outer air, no herniation was observed. After the wound had granulated, skin was grafted. This was taken from the amputated leg, which had been kept in the ice-box at 34° F for two weeks. Successful grafting occurred in 80 per cent of the grafts applied. Gordon-Taylor saved the epigastric artery whenever possible, so as to preserve the blood supply to the rectus muscle.

Sequelae encountered in these four cases are recorded, so that they may be avoided by future operators. In Case 1, we had a rather severe infection

I believe that it came through the vault of the vagina which may have been opened at operation. At any rate the abscess discharged through that area. There had been no preparation of the vagina preoperatively, but in Case 3, we took this precaution. It would seem to be a wise prophylactic measure in female patients.

It was not surprising to have bladder difficulty following operation in these patients. We adopted tidal irrigation as simpler than multiple catheterizations. After two to seven days it was possible to remove the apparatus without further trouble resulting. Case 3 did not require this treatment.

It was thought that detaching the levator ani muscle on one side might upset the evacuating function of the rectum, but this was not the case. At first, we believed that something should be done to constipate the bowels in order to avoid infections. Opium pills were given for this purpose. In the later cases no medication was given. The bowels returned to normal function after three to seven days in our cases, and became regular without medication.

No prosthesis can be fitted easily to this stump. The patients quickly learn to use crutches, and get around well by this means. They learn to adapt themselves to sitting on the involved side. The younger patients, according to reports, adjust themselves more quickly and successfully.

The most annoying of the sequelae was the development of a phantom limb by these patients. They all had it in varying degrees, and proportionate estimation of its nuisance value. This subject is of great interest by itself. We are now making an investigation of it. Attempts to modify this phenomenon by treating the severed sciatic by different methods failed to make any appreciable effect on the outcome.

The fact that we could carry all four of our patients through this severe type of operation without having had any previous experience in it, indicates that it is a feasible procedure for the surgeon when the necessity arises. Fortunately, the necessity for this major mutilation is rare. It has been undertaken for sarcoma of the innominate bones or upper femur, extensive sarcomata of the muscles of the thigh and pelvis, giant cell tumors of the pelvis, and tuberculosis and osteomyelitis of the pelvic bones.

The mortality as given in Gordon-Taylor's first report, of 59.5 per cent, should be reduced. The mortality of 33 per cent, of his later report, can be improved upon. To the precautions advocated by former surgeons, we would add gentleness and lack of urgent speed. The surgeon should keep on moving, however, and not be slow without some object. The availability of blood plasma should be added to the safety factors when such an operation is contemplated.

The results of this operation will be improved when surgeons realize that the operation can be undertaken with relative safety. They will no longer hesitate to offer their patients a chance for cure, which they now deny them. The first two patients of our series were advanced malignancies. They were afforded palliation and comfort. The third patient seems to have a hopeless situation. It may be that this is one of those rare, so-called benign metastasiz-

ing adenomata of the thyroid. Certainly, to date, there is nothing to indicate a further progression of the disease. In Case 4, the draining focus has been eliminated, but the ultimate cure of the mental state must await the test of time. These end-results are not good. But they hold a hope that, in the future, somebody may be benefited by this type of surgery.

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DISCUSSION—DR T. C. DAVISON (Atlanta, Ga.) I performed one operation like this 20 years ago or more, and it has never been reported. I did not know then that such operations were so rare. This patient was 70 years of age, and he had been burned severely on the anterior surface of the right thigh and right groin in infancy, which resulted in extensive scarring. Portions of this scar had degenerated and developed an extensive carcinoma with involvement of the lymph nodes. It was very evident that a hip joint amputation was indicated, therefore, a high incision was made above Poupait's ligament and the abdominal peritoneum was pushed upward to the bifurcation of the abdominal aorta. The external iliac artery was ligated and the internal iliac was taped temporarily. The enlarged nodes were removed from the bifurcation of the abdominal aorta downward. The bone was saved off, including the pubic ramus, crest of the ileum, and the acetabulum. A posterior flap from the gluteal region was used to cover the stump. The patient lived for seven years and died of pneumonia.

THE SURGICAL CORRECTION OF MANDIBULAR PROGNATHISM*

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PROGNATHISM is a deformity characterized by an abnormal protrusion of the mandible. The broader part of the lower dental arch lies opposite the narrower portion of the upper arch, causing a malocclusion varying with the degree of the deformity. The protruding chin, with the massive jaw and heavy lips, often results in a very displeasing appearance, which primarily causes the patient to come for surgical aid. It may be due to actual hypertrophy of the bone, errors in the eruption of the teeth, premature extraction of deciduous molars, or to fractures or contracting scars of the face and neck.

Orthodontic treatment should be tried if the patient is under 16 years of age, unless the deformity is very severe or does not involve the dental arches.

There are two general groups of surgical methods for correcting this deformity. One deals with a simple section of the bones on either side, with a posterior displacement of the mandible, held in its new position by fixation of the dental arches.

Various levels of sections are advocated by different surgeons. The cuts can be made in the neck, at various levels of the ramus, or at the angle. A section through the neck is only indicated if the deformity is due to a malunion of a fracture in this area. A section through the angles is of little value since it permits very little backward movement of the body of the mandible. Cuts at various levels of the ramus can be undertaken safely, with care, and have the advantage of avoiding an opening into the mouth and breaking the continuity of the dental arch. The chief objection to these operations is that there may be an interference with function because of the backward displacement necessary.

The second group of operations deals with the removal of sections of bone from the ramus or the body of the mandible. Since very few of these cases have an elongation of the ramus, any shortening with the posterior displacement necessary for the correction of the deformity will cause interference with function.

The most desirable operations deal with the body of the mandible itself. The corrections resulting from the removal of sections of bone take care of both the protrusion and the widening so often seen. The site of operation depends to a great extent on the denture. If all of the teeth are present, the second premolars can be extracted. Spaces caused by the separation or loss of premolars or molars can be used, providing there are teeth behind to hold the splints necessary. In the appended cases extractions were necessary to secure the space required.

* Read before the Southern Surgical Association, Pinchurst, N. C., December 9-11, 1941.

The main purpose of this communication is to call attention to a simple method of fixation of the three fragments of the mandible after resection and

CASE REPORTS

Case 1—White, female, age 26 Marked protrusion of the lower jaw with a mal-occlusion (Fig 1) The lower first molars were occluding against the upper premolars



FIG 1—Case 1 Mandibular Prognathism Note protrusion of the mandible, with the heavy lips



FIG 2—Case 1 Roentgenograms of mandible before operation All of the teeth are present Note that the incisors tend to turn in and that there is an open bite The lower first molars occlude against the upper premolars There is an hypertrophy of the mandible

The incisors, both upper and lower, tended to turn in The body of the mandible was hypertrophied, all of the teeth were present (Fig 2)

Casts were made of the denture (Fig 3) The first molars were then extracted and the spaces retained by placing caps between the teeth The orthodontist placed bands around the second lower molars, with a short tube attached to the buccal surface Bands

MANDIBULAR PROGNATHISM

were placed around the premolars on both sides, with a tube soldered to the outer side. The tubes permitted a square threaded-rod to pass through. The cast was now cut in the region of the first molars and the correction made. Careful measurements were taken of the width of the segments removed (Fig 4).

Bands were placed around the upper first molars and first premolars with a rod soldered to the buccal surface.



FIG 3—Case 1. Casts made of the denture before operation, to determine the location and extent of the operation.



FIG 4—Case 1. Occlusion of the casts after the portions were removed. The width of the pieces removed was carefully measured. The remaining malocclusion was later corrected by the orthodontist.

Under general anesthesia, an incision one and one-half inches long was made in the skin under the margin of the mandible, over the area where the tooth had been extracted. The mandible was exposed and the periosteum marked with brilliant green (alcohol 5 per cent solution) according to the predetermined measurements. Two holes were drilled through the bone near the lower margin 0.5 cm from the marks. A silver wire was threaded through the holes, with the ends to the outside. The periosteum was incised and the section of bone removed with a saw. A similar procedure was carried out on the other side. The four saw-cuts were made almost completely through before the continuity of the bone was broken, in order to control the bone and secure even accurate cuts. Care was taken to avoid stripping the periosteum back from the margins. The pieces of

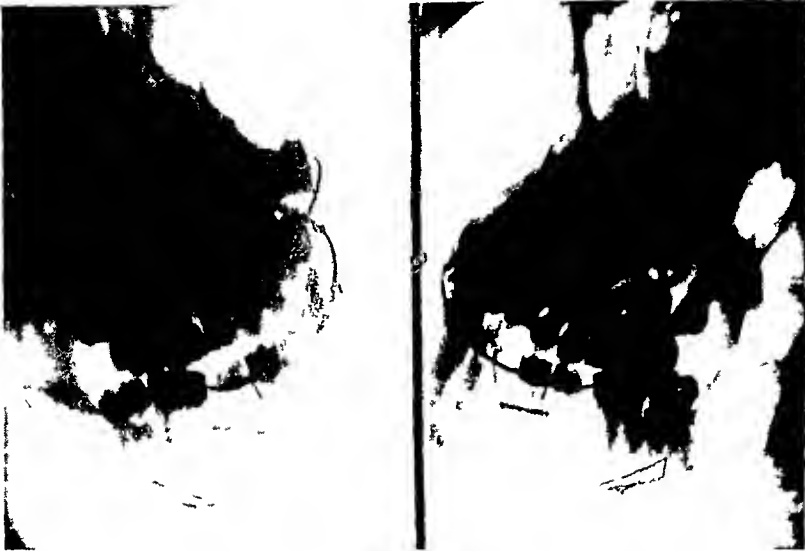


FIG 5—Case 1 Two weeks after operation. Note the shadows of the silver wires. The angle at which the pictures were taken makes it appear that the margin of the tooth is in the cut. There was sufficient bone near the roots of the teeth to avoid injury.



FIG 6—Case 1 One year after operation. The teeth occlude. The small scars visible are not objectionable to the patient. The chin has been adjusted to a more normal position.

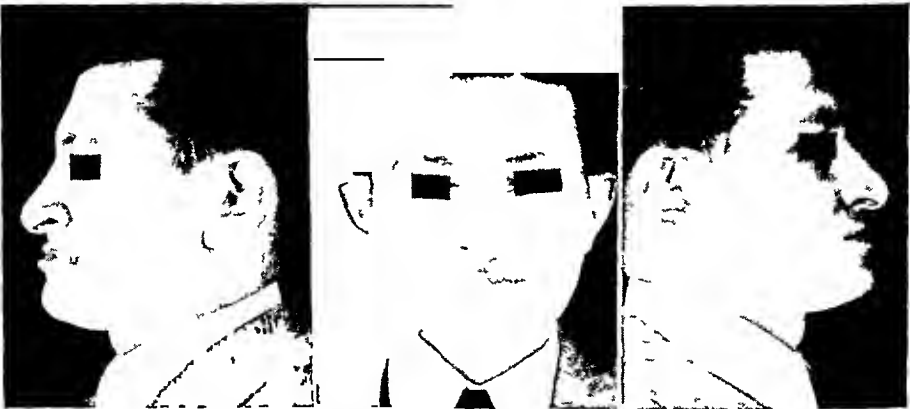


FIG 7—Case 2 Mandibular Prognathism. Patient did not care so much about his mal occlusion as about his appearance.

bone were removed and the square rod inserted. Nuts were placed on the threaded ends, which permitted firm approximation. The silver wires at the lower borders were tied firmly. The mucous membrane was approximated inside the mouth. A horsehair drain was inserted from the skin side and the incision closed with horsehair. The ends of the wire were turned to the outside (Fig 5).

The following day, after the patient had reacted from the anesthesia, the lower jaw was fixed to the upper by wires, connecting the two bars.

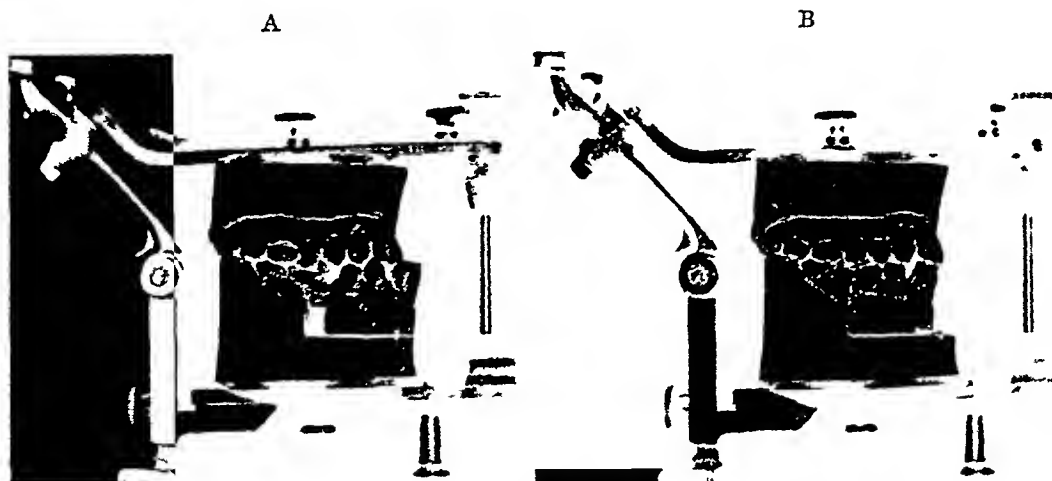


FIG 8—Case 2. Casts were made of the denture of both jaws and placed to show the occlusion. A section was then removed to secure proper occlusion. (A) Segment moved out to show the amount of cast removed and to show the condition as it existed. (B) Segment pushed back to show the correction. The width of the segments removed was carefully measured.



FIG 9—Case 2. Golden bridge and caps, with the tubes soldered in place, were made for the teeth on the cast of the lower teeth. (A) The segments pulled apart to show the position of the parts as they would be on the teeth before operation. The two rods, seen in the lower part of the cast, were used to assure correct movement and adjustment of the fragments. (B) Segments approximated and the bolts fastened in position, as they would appear after the operation.



FIG 10—Case 2. Roentgenograms of lower jaw two weeks after operation showing the fragments held in position by the apparatus. The wires in the lower borders are barely visible because the wire was of very fine gauge being steel.

Recovery was uneventful. The drains were removed in two days, and the sutures in seven days. The teeth were cleaned and inspected every three or four days, when the wires between the bars were changed. The patient was fed a high calorie liquid diet, and only lost three pounds.

After three weeks, the mandible was freed from its immobilization to the upper jaw and the patient given a very soft diet. Seven weeks after operation the apparatus was entirely removed. The silver wires were removed after four weeks, and the openings healed, leaving small adherent scars. There was some motion in the front segment for a few months, which gradually disappeared as the callus became firmer. The lower lip and a part of the chin lost sensation, which returned in a few weeks and became entirely normal in three months. The teeth all appeared viable (Fig 6).

COMMENT—The immobilizing apparatus was applied to both jaws, making it difficult to feed and care for the patient. The absolute immobilization made it likely that the callus was slow in forming. The wires turned through the skin caused scars, which were not completely satisfactory although massage finally made them inconspicuous. In view of these objections, a simpler apparatus was planned for the following case.

CASE 2—White, male, age 22. Protrusion of the mandible with malocclusion (Fig 7). The second premolar was missing on the left side. There was a hypertrophy of the body of the mandible. Casts were made and sections removed to give the desired occlusion. Measurements were taken of the segments (Fig 8). A golden bridge was made to fit the teeth in front of the second premolars, with a short tube soldered on the buccal surface. A cap, with a tube soldered to it, was made for the first molars. The ends of the short tubes on the molar caps held the nuts firmly set. A short bolt was passed through the tube on each side, which could be screwed into the nut (Fig 9).

The premolar on the right was extracted, and the operation performed ten days later. We did not hesitate to cut through the newly healed gum, since fractures will heal under similar conditions. The bridge and caps were soldered into place.

Under general anesthesia, incisions, one and one-half inches long, were made through the skin, exposing the mandible at the selected site. The measurements were marked on the bone. Drill-holes were made near the lower margins about 0.5 cm from the line of the cut, and steel wires passed through, with the ends to the inside of the mouth. The sections were now removed, the bolts passed into the tubes and tightened with a screwdriver. The wires were tied to the inside of the mouth. Horsehair drains were placed in the incisions, which were closed (Fig 10). The drains were removed in 48 hours. The patient was discharged four days after operation. The skin sutures were removed in seven days, with *per primam* healing. The patient was given a liquid diet for four days, after which a very soft diet was ordered. Chewing was not encouraged, but he could talk as much as he desired. After the second week chewing gum was advised and a diet of soft foods, which required some chewing, was permitted. It was felt that the stress of use would speed the formation of the callus. The loss of sensation began to disappear after the third week, and sensation became normal during the third month. In five weeks, the wires were removed with ease. In eight weeks, the bridge was removed (Fig 11). The patient had some false motion and a slight tendency to open-bite, which disappeared as the bones became firmer (Fig 12).

COMMENT—The advantages of not wiring the jaws together are apparent. The teeth could be easily cared for by the patient himself. The liquid diet was reduced to a short time, so that the patient did not lose weight or become unhappy. He could go about his work after the second week. The wires being turned into the mouth prevented the formation of a sinus and gave

perfect healing There is no danger in breaking the continuity of the mandible The nerves regenerate rapidly and the teeth do not lose their vitality This method permits a careful performance of the operation on the casts, with a definite knowledge that the parts will come together as desired Infections from openings into the mouth are, apparently, not to be feared Neither patient was given any of the sulfa drugs

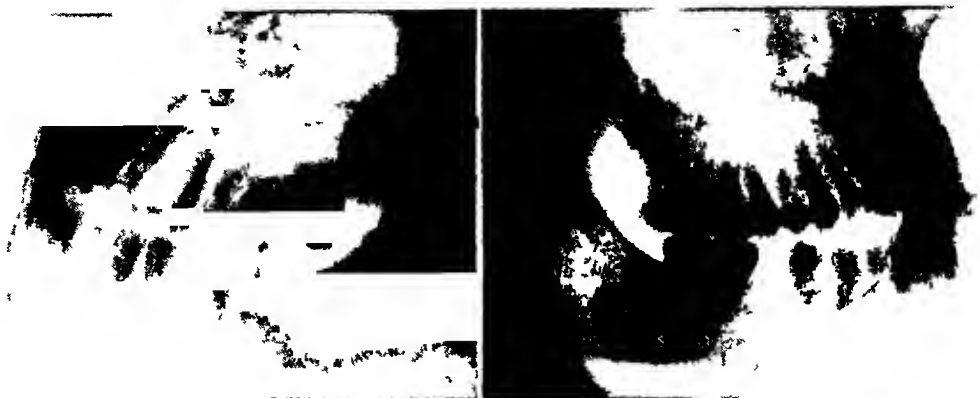


FIG 11—Case 2 Roentgenograms of lower jaw eight weeks after operation The fixing apparatus had been removed together with the wires The union was firm enough to permit use, even though there was a little false motion



FIG 12—Case 2 Ten months after operation There is still some fulness in the soft parts, which is gradually disappearing The chin is now in a fairly satisfactory position Union is firm

CONCLUSIONS

Operations upon the body of the mandible can be performed without danger of permanent loss of sensation or of the vitality of the teeth

A simple bridge attached to the teeth will hold the three sections of the mandible together satisfactorily

Wire suture at the lower margins of the cuts prevent a tendency of the posterior fragments to turn, and will not cause serious damage Fine steel wire is better than silver wire, since it has more strength in proportion to its diameter

The author wishes to express his appreciation to Dr Meyer Eggatz, who prepared the casts and made the appliances for the first case, and to Dr G W Gaver, who conceived the apparatus, and made the casts for the second case

SPRAINED ANKLES*

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"A SPRAIN IS WORSE THAN A FRACTURE" is an expression one has often heard. Scientific minded people are inclined to disregard all such old fashioned phrases as being of no significance. However, the writer has come to regard these expressions as having some merit until proved otherwise. Of course, it is not true that a sprain is worse than a fracture. That would be ridiculous, but there have been many, many instances in which an injury to an ankle or a wrist or shoulder was called a sprain, when some other lesion was present, and as a result, the simple treatment for sprain was found to be inadequate.

The crux of the whole situation lies in diagnosis. If an ankle is truly sprained, the lesion is a very simple one and will promptly respond to simple treatment. The injury consists of stretching of the external lateral ligament of the ankle joint with perhaps a rupture of a few fibers, but without complete rupture of the ligament, and without rupture of the astragalofibular ligament. Such a lesion, if properly strapped will give little further trouble, should not have a tendency to recur, and, all-in-all, is a minor accident.

However, there are many cases in which the external lateral ligament of the ankle joint is completely ruptured, the astragalofibular and tibiofibular ligaments are also torn, and in which the astragalus becomes dislocated. There may be a very slight fracture at the lower end of the fibula, or the fibula may be intact. The point, however, is that the lesion is primarily a dislocation of the ankle, which has become reduced before being seen by the doctor and before being examined roentgenologically. Such a lesion, if treated by simple strapping, will be stubborn. The patient will not get well promptly, and even when he has returned to work, there will be a tendency for the "sprain" to recur. The patient will consider that he has a weak ankle. Watson-Jones¹ has pointed out that these are the ankles which remain a little thicker and sprain easily.

There are several ways in which the diagnosis of this more serious lesion can be made. The bleeding is always more severe than in the ordinary sprained ankle, and consequently the swelling is greater. The swelling may extend to the opposite side, although there will be no tenderness on the inner side. There is, usually, in these cases, tenderness over the anterior tibiofibular joint, as well as tenderness around the lower end of the fibula, and not just below it. However, there is one certain way of determining which lesion we are dealing with. If a few cubic centimeters of novocain are injected around the lower end of the fibula, that is, below and to the sides of the external malleolus, and then an anterior posterior roentgenogram is made with

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941.

someone holding the foot in as much supination as possible, one can easily tell whether there is a tendency for the astragalus to dislocate or not. If rotation of the astragalus takes place under these conditions, we are dealing with a partial or complete dislocation of the ankle, and not with a sprained ankle. If movement of the astragalus does not occur, then the ankle is merely sprained. We have tried this maneuver without the use of novocain and failed to produce movement of the astragalus, but later, with novocain, did demonstrate the dislocation when the pain had been eliminated.

We, therefore, believe that one cannot be sure unless novocain has been adequately injected, and a real attempt made to supinate the foot before the roentgenogram is taken. These cases, that is, those in which the astragalus can be rotated, cannot be adequately treated with strapping, but must be placed in a plaster encasement, preferably a skin case, with the foot neither supinated nor pronated, and at a right angle to the tibia. A walking iron or heel can be applied early and the patient permitted to walk.

Sir Robert Jones, long ago, pointed out that it was improper to treat a sprained ankle with plaster. This is true if the ankle is merely sprained. His reason was that spasm of the peroneal developed, and the net result was spasmodic pronation of the foot. However, we have not seen this occur in these more serious lesions. Therefore, we would turn to the original statement that the whole crux of the situation lies in the diagnosis, followed by adequate treatment for whatever lesion is present. The same remarks could apply to the employment of novocain. If an ankle is merely sprained, novocain injection is a good treatment, but if a more serious lesion is present, it is entirely inadequate, and great damage will be done if the patient is permitted to get about without proper support.

We have had the opportunity to make some experiments on two fresh cadaver specimens. In one, a roentgenogram was taken with the ankle supinated as far as possible, and no dislocation of the astragalus was observed. Then the calcaneofibular ligament was cut, again the ankle supinated, and this time a very trifling amount of rocking of the astragalus was demonstrable. Following this, both anterior and posterior astragalofibular ligaments were cut and, with a slight amount of supination, the astragalus was rotated markedly. In the second case, we first cut the astragalofibular ligament without cutting the calcaneofibular ligament. Again the astragalus could not be dislocated, but when the calcaneo-astragaloid ligament was cut in addition, severe dislocation occurred.

It appears, therefore, if this small number of experiments are of any value, that it is necessary for both groups of ligaments to be torn before the dislocation can occur.

REFERENCE

- ¹ Watson-Jones, R. *Fractures and Other Bone and Joint Injuries*. 2nd ed. Baltimore, Williams and Wilkins Co., 1941.

DISCUSSION—DR. CLAY RAY MURRAY (New York, N. Y.) I should

like to take this opportunity to express my appreciation of the privilege of being your guest and of the pleasure this occasion gives me. I feel impelled to comment on one point in Doctor Carothers' paper.

Doctor Carothers has called attention to a very important fact, that the recurrent sprained ankle is not an ordinary sprained ankle, and that the exact diagnosis cannot be made without using special diagnostic measures. But I think he has, more or less, "missed the boat" on the point of the exact nature of recurrent sprained ankle. He has demonstrated that cutting various ligaments has the effect of producing instability in the ankle joint mortise. I very much doubt, on the other hand, that the astragalofibular ligaments are ever torn in these ankle sprains. I know, however, that the ligaments of the inferior tibiofibular joints may be torn without any roentgenographic evidence of diastasis in the joint by the ordinary technic for ankle joint roentgenography, unless novocain is injected or an anesthetic administered, and the attempt is made to spread the tibia and fibula apart by manipulation of the foot. An actual spread, with tilting of the astragalus, can then be made evident. It is my impression that this is the lesion with which we are dealing in the living human being in cases of recurrent ankle sprain, and I believe the tests described should be made in any fresh ankle sprain in which pain and tenderness over the inferior tibiofibular joint can be demonstrated, or in which a hemarthrosis of the ankle joint exists. I must admit that there may be other combinations of ligamentous tear which might produce the same effect, but I assume Doctor Carothers is discussing this type of sprained ankle as it occurs clinically, outside the autopsy room, and this is, I believe, due to the lesion which I have described.

DR GEORGE E BENNETT (Baltimore, Md) Doctor Carothers' statements are quite true, and he has emphasized a proven experimental point, namely, that tearing of ligaments is productive of serious disability. I think it would be wise for Doctor Carothers to extend his research a bit further. My impression is that some of the very serious so-called sprained ankles are due to a tearing of the tibiofibular ligament and a spreading of the joint mortise. I would like to suggest to him that after the division of the ligament, a roentgenogram be made with the foot in full plantar flexion and in full dorsiflexion, to ascertain the mobility of the fibula after the ligaments have become detached. On a number of occasions I have operated upon joints of this type, reconstructing the tibiofibular ligament to relieve this painful relaxation.

DR ISIDORE COHN (New Orleans, La) It is unfortunate, I think, that we often forget classic work done in the past. Ross and Stewart, in Philadelphia (1911), undertook to study the question of sprains and sprain-fractures, experimentally. As a result of their experiments they concluded "The integrity of joints is maintained by strong ligaments, and in order to have a luxation one or more of the strong ligaments must give way, we have shown that ligaments themselves do not give way, but the bony tissues to which they are attached give way, therefore, we think that probably all luxations are permitted by the primary occurrence of a sprain-fracture." This experimental work was corroborated by their clinical experience.

My own clinical experience has led me to feel that, in most instances, a sprain-fracture occurs rather than a laceration of ligaments about joints. I believe that the bony prominences to which the ligaments are attached have less tensile strength than the ligaments themselves, therefore, when the arc of motion of a joint is carried beyond the normal range, a small fracture

occurs more often than a tearing of ligaments. I believe that most sprains occur in the mind of the doctor and not in the body of the patient. I believe that most sprains are fractures and that, if we have 10 roentgenograms enough, in various positions, they will confirm this statement, as tiny fragments of bone can be demonstrated very often. These tiny fragments of bone break off more often than we think.

I might remind you that the leather hinges, which were used at one time on the barn door, were held in place by nails, and if the door were torn away from the side of the barn the wood would break off before the straps would tear.

I believe it is worth remembering that ligaments have more tensile strength than the bony prominences to which they are attached.

If we will study the cases carefully enough we will find that most of the sprained ankles are in reality fractures about the ankle. When in doubt, cases should be treated as fractures and not merely as lacerations of the ligaments about joints.

DR RALPH G. CAROTHERS (Cincinnati, Ohio, closing). I feel highly honored that the shortest paper I ever read before the Southern Surgical Association has had so much discussion. Doctor Cohn brought in some old farm problems, and I will bring in the sea. A sailor will tell you that if a long rope is fastened between boats which are moving, that rope will snap in the middle before it will injure the spar to which it is attached, but if you have a close-coupled situation you are liable to pull half the boat off. You will probably snap the external ligament in which there is a lot of play, or, the other way, you may snap off the malleolus on the inner side.

Doctor Murray is right. I have only had two fresh cadavers. It is necessary to have a fresh specimen, you cannot wait until rigor mortis sets in. Most patients will tell you they heard or felt something "pop," whereas with an ordinary sprain they do not have that feeling, and one case looks as bad as the other when they come in.

MASSIVE REPAIRS OF BURNS WITH THICK SPLIT-SKIN GRAFTS *

EMERGENCY "DRESSINGS" WITH HOMOGRAFTS

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THE REPAIR of massive burns with thick split-skin grafts as may be seen in the illustrations is the main subject of this report. But because of new interest stimulated by a realization of the numbers of burns that may occur in combatants and civilians, and queries such as by Dr. Walters in the discussion, it has seemed possibly worth while to summarize, again, the procedures that have already been found of value in repairing a good-sized series of deep burns.

One fundamental of extreme importance is the general care of each individual patient and the avoidance of pain. Burns seem so terrible to most people, and even more so with women and children, subject to them from military attack, that a new dread is formed, and a point of morale comes up for the military forces as well as the civilian. This may be one of weakness in general, but it might be strengthened if it could be made known that burns and their deformities can and will be taken care of. This point of morale must be important, also, in the enemies' eyes, or there would not be so much effort on burn-producing tactics. Besides the agony at the time of the burn, there is an added amount of it, if the patient does survive, when the wounds granulate and new nerve endings form.

Other summaries of this work have been made,¹⁻¹⁴ and quotations here are from them. While it is recognized that little of the good that might be wished for has been accomplished, it still seems best to start from what is already known. There is vast room for improvement, but possibly the most good for the individual will come from hard work, cleanliness, gentleness and simplification of effort. The expected new instances of burns will undoubtedly stimulate investigation as to their prevention, as to the most direct care for the patient immediately after the burn, and subsequently in relieving deformity. The pathology may be slightly different in burns from different causes, but the methods that have been found successful in repairing the resultant wounds in civil life can be applied to military casualties.

At the present time, with careful removal of grafts, so that prompt healing of the donor sites occurs, most patients can supply enough skin for their repair. As many as five "crops" of thick split-grafts have been taken from

* Presented by motion pictures before the Southern Surgical Association, Pinelhurst, N. C., December 9-11, 1941.

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the same donor area, 220 square inches have been transferred at one time, and 600 square inches have been grafted in a single patient (Figs 1-4). As interest in the subject becomes more widespread, and as the possibilities of repair with thick split-grafts are recognized, new authors appear with worth while contributions, but often with the introduction of new terminology, and sometimes without realizing what already has been accomplished.

"When the full thickness of the skin is destroyed by a burn over a large area, an open wound results, and, unless there is early replacement of the lost skin by skin grafting, healing will occur by contraction of adjacent tissue and by 'scar' epithelium, or permanent healing may never occur (Fig 4).



FIG 1—(A and B) Total loss of skin of both thighs and buttocks. Twenty six large split homografts from 26 donors used as 'emergency dressings' before any autografts were made, thought to be life saving in this instance. Different grafts persisted from three to 11 weeks.

Care of Open Wounds—"Almost any treatment that promises as little work as possible is apt to become popular, but, so far, no application has been found that will produce normal skin and, when it is claimed that a certain preparation will insure complete healing without scarring, it is apparently not realized how healing occurs in superficial and in full-thickness losses of skin.

"If there is rapid healing and return to function following a burn without much scarring or deformity, this simply means that the full-thickness of

the skin has not been lost, and that regeneration has occurred from the deep glands in the derma, much the same as occurs in the donor site of a thick split-graft

"It has been observed that these struggling cells are easily killed by chemical, bacterial, or mechanical trauma. Therefore, it appears that cleanliness,

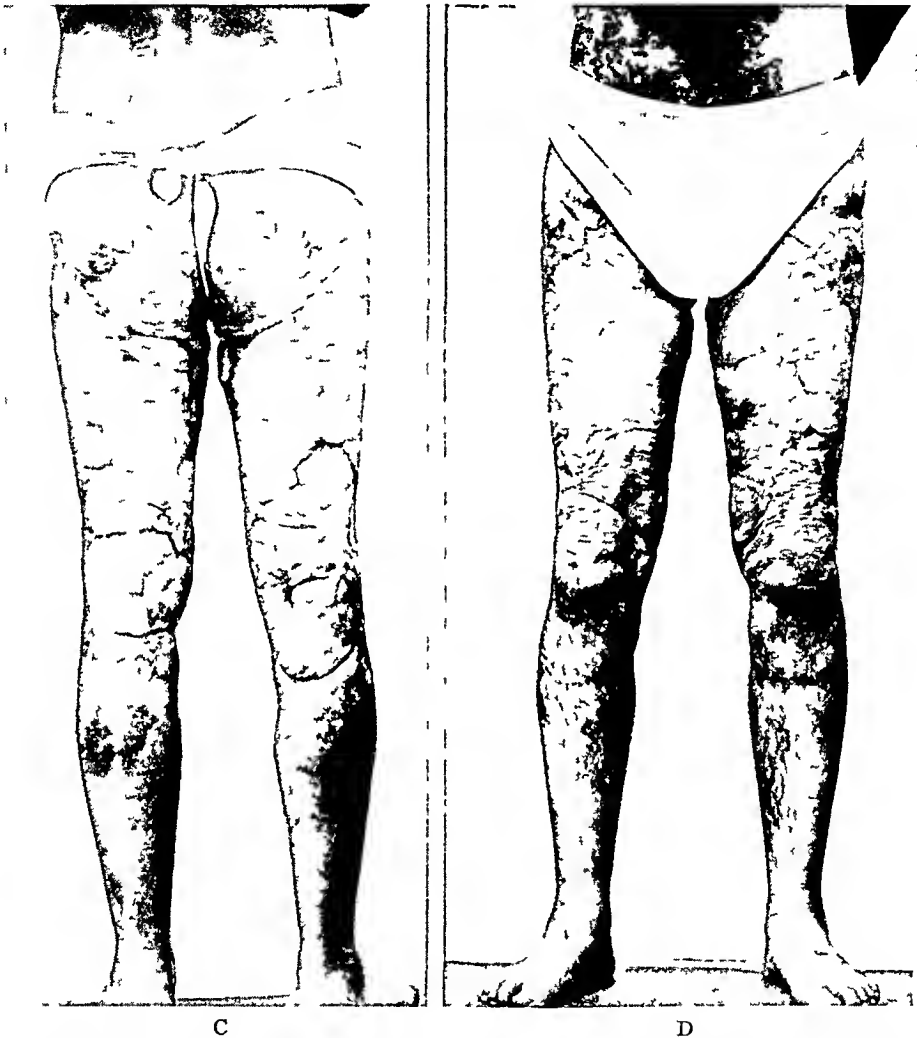


FIG. 1—(C and D) Total restoration of function, five operations. 600 square inches of skin taken from back and abdomen—four "crops" from same areas and one "crop" 19 days after the preceding one. Scars on donor sites hardly noticeable. Donor sites on back inadvertently cut off in the reproduction.

protection, and the avoidance of strong chemicals will best promote this type of healing, and these objects of treatment seem to have stood the test of time."¹³

Open Surgical Drainage—This is the essence of local treatment, using soap and water and saline dressings or saline baths (Fig. 8). Chemotherapy is added to this, and sulfadiazine or other sulfa-drugs are sprinkled on the area before saline packs or other dressings are applied. The total dose of the drug per 24 hours, according to Perrin Long, should not be over 15 Gm a day for an adult. Dressings may be kept wet, or open irrigations carried out with a 1 to 2 per cent suspension of sulfanilamide.

The object, besides saving life, is to get the areas clean quickly, so that skin grafts can be applied before contractures have occurred, and before debilitation and pain have developed beyond control (Figs 1, 2, 4, 8 and 9) When wounds are clean and free of cellulitis, the wet packs may be discontinued. The wounds are still cleaned at each dressing, and are sprinkled with sulfanilamide, and wrapped firmly with fine-mesh gauze containing sulfa-drugs in an ointment or aquaphor-like base, or an antiseptic ointment such as merthiolate. The wet dressings are changed at least every 24 hours, but

E



F

FIG 1—(E and F) Laborious, but necessary, method of dressing, to insure growth of grafts and healing of donor sites. Fine mesh gauze roll has "snubbed" grafts in place.

the wounds may go longer with the grease-gauze dressing. Any proven advance in chemical or biologic cleaning of wounds can be added to this general outline, but the important point is to recognize that mechanical cleansing and drainage are essential for any plan and, also, that innumerable antiseptics will be recommended.

Fine-Mesh Gauze—This is a fundamental in dressing all raw wounds (Figs 1 and 7). The mesh of this gauze is No. 44, and one or two layers of it are placed next to all open wounds, so that granulations will not grow up through the coarse meshes of overlying surgical gauze, stick, and cause pain.

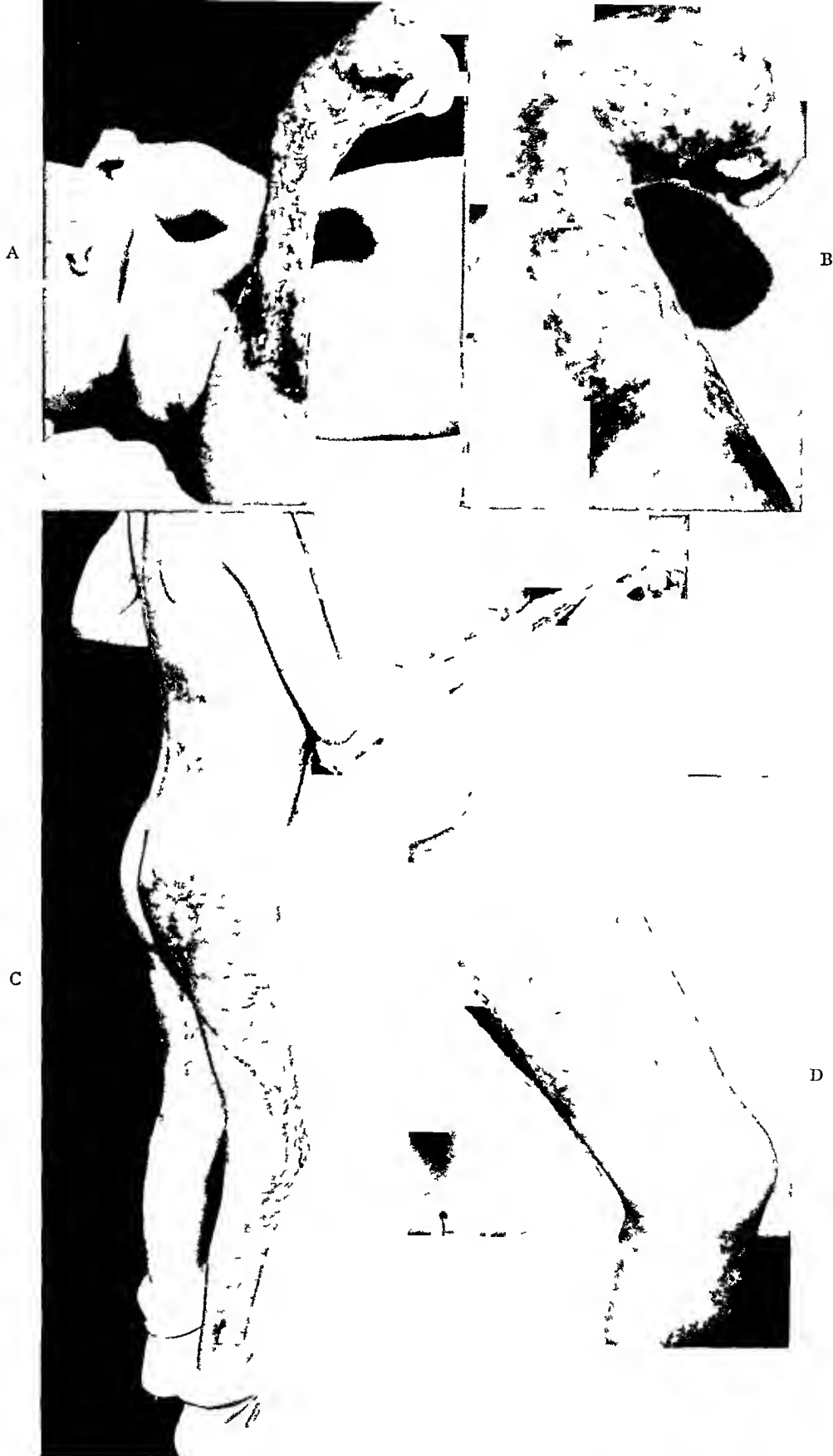


FIG 2—(A) Total burn of hand and forearm. Patient intractable to the point of having had amputation considered. (B) Total restoration with split grafts, without repairing deformity. One operation. Performed with autografts at same time leg was covered with homografts from father. (C) Completely healed only two operations, with his own grafts from the back and abdomen. Hand opened out and further grafting at second operation, when leg was covered with his own grafts. (D) Donor site of homografts on the father.

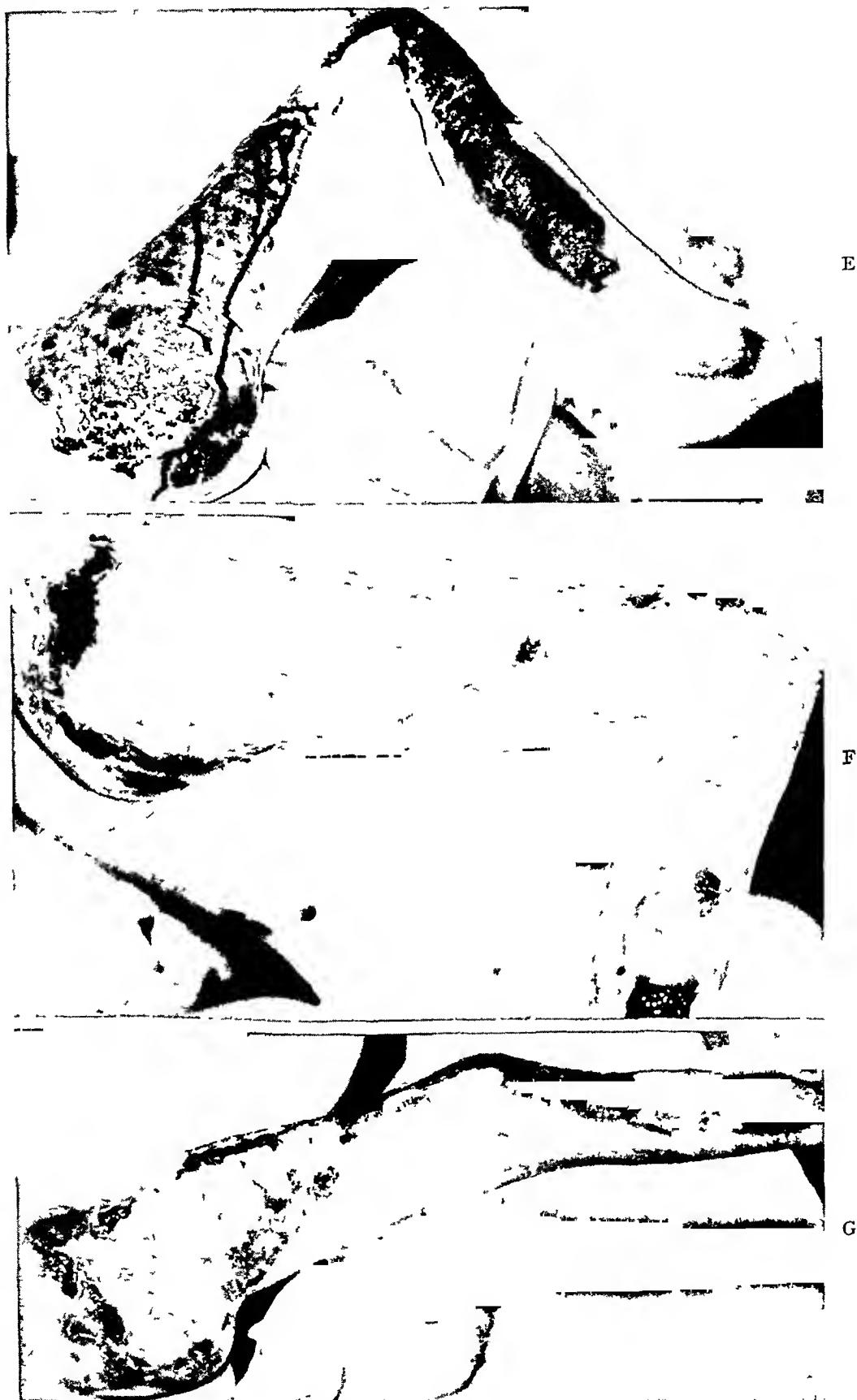


FIG 2—(E) Leg of same patient. Ninety degree flexion deformity from secondary contracture. Death may occur in this stage, and the work of cleansing the areas and getting patient ready for operation, at times, seems insurmountable. (F) Leg "dressed" in split homografts from father. Complete "take" and coverage, three weeks postoperative. (G) Homografts still present after six weeks, but beginning to melt away. Improvement can be measured by the fact that the patient has opened his 90° flexion deformity spontaneously. Whole area restored later, in one operation, with thick split grafts from back, as shown in Figure 2 C.

It may be used as it comes for wet dressings, or have greases incorporated in it. One of the easiest ways is to have the ointment soaked in a full roll, store it that way, and use it from the roll, especially for extremities. Plain vaseline is not used because of a tendency to macerate, but almost any powder in vaseline, sulfanilamide, xeroform, scarlet red, boric, *etc.*, will prevent maceration of the skin.

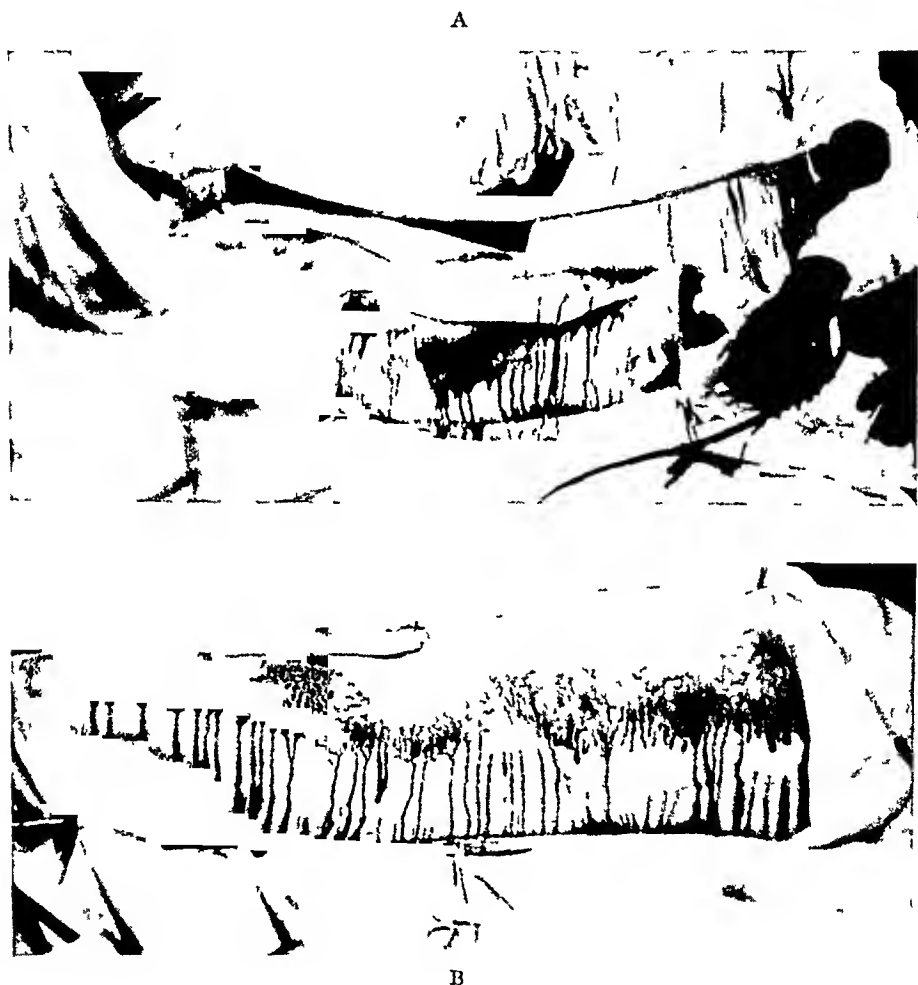


FIG 3—Cutting large, thick split grafts. (A) Very large grafts can be obtained from large patients. One graft, 36 inches long and four to five inches wide is seen held above the patient. Another one is being detached, 18 inches long and five inches wide. (B) Donor site of a single large thick split graft. Total amount removed at this operation, 220 square inches. Same patient as Figure 4.

Firm Pressure or Elastic Dressing—This may be of great advantage, and discolored, edematous granulations may be flattened out into a firm, bright red surface without cauterizing or cutting them away. Cotton mechanic's waste may be incorporated in the dressing as a medium of pressure (Figs 1 and 7).

Saline Bath—This bath of all or part of the body has often been a life-saving measure, many patients are extremely grateful for the bath and realize their first comfort in it. The bath is not easy to manipulate (not even possible some places), but its technic is not as difficult as it sounds, and it may

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be the easiest way to get the cleansing done. The water is kept comfortably warm, up to 5 per cent salt may be used and cleanliness but not sterility is aimed at. Soap cleansing and gentle débridement of dead tissue can be done with less pain when the patient is in the bath. If there is any unfavorable



FIG. 4—(A and B) Repair of huge burn scars and ulcers of legs with thick split skin grafts, transferring 220 square inches at one operation. Same patient as Figure 3.

reaction, it is omitted. The bath may have the important result, that most secondary contractures will be straightened out by the voluntary effort of the patient without the use of traction or restraints (Fig. 8).

When out of the bath, further fine-mesh gauze dressings, either wet or greased, are used, and a covered bed makes nursing easier. Overhead lights may supply warmth, but too much heat is not advisable.

Large open wounds seem impossible to sterilize, but careful evaluation of the general condition and of the gross appearance of the granulations, sur-

rounding tissues and the absence of cellulitis usually suffices for the determination of the time for operation, and many deep burns are ready for grafting in three weeks' time. In them, general debilitation is worse, the fluid loss is, of course, greater, there is more chance of deformity and more chance of damaging some underlying structure in the operation, so that a very large wound, from the possibilities of repair, does present many of its own problems not so troublesome in small wounds.

Bacillus pyocyaneus is very frequent in large wounds, especially if they have been uncleaned over a long period, and though it does not appear to hurt the patient or the wound, it is exceedingly bad for skin grafts. If the open surgical drainage and sulfanilamide does not suffice, then being sure to get rid of all caked debris with soap, water and forceps, and the application, one or two times a day, of 5 per cent gentian violet or mercurial antiseptic may help.

Infected tannic acid membranes occur in practically all deep burns where this treatment has been used, and the disposal of the membrane and control of the infection is always a problem. The membrane may be opened in several places and any loose areas detached and then powdered sulfa-drugs and packs used as outlined above, or the drug in ointment applied, if there is not too much discharge and cellulitis. Open surgical drainage plus chemotherapy, in other words, is again the treatment. If one thinks that toxins might be released by the soaking of the membrane, hypertonic saline could be used. If the tannic membrane is clean, as it may be on a superficial part of the burn, it may as well be left until it drops off, even if this takes several weeks, because cutting or pulling it off only disturbs the healing.

While on the subject of infected tannic membranes, it may be well to state that burns of the hands and face and the genitalia do best with open surgical drainage treatment from the start. Any treatment any place in the body should be preceded by careful cleansing with soap and water, debridement, and ether as a solvent if necessary, and all burns could be treated with open surgical drainage and chemotherapy. This is important in the areas mentioned, because the hands should be allowed movement and grafted early, the face seems to heal best and rapidly with open drainage, and there is not so much chance of damage to the eyes, and the genitalia almost always require open drainage anyway, if the burn is deep.

The general condition of the patient is directly reflected in the wounds, and, of course, should be considered primarily in all instances. Gentleness in all manipulations is always an essential of the care. In this stage, anemia is usually present, and frequent whole-blood transfusions may be necessary. Adequate diet, protein, and vitamin intake are important. For infection that is not controlled with the local treatment, sulfanilamide is given by mouth as indicated.

Thick split-skin grafts of from one-half to three-fourths of the thickness of the whole-skin are the most useful in making repairs of raw surfaces. These could be called "thick Ollier-Thiersch grafts" but the original Ollier-Thiersch

THICK SPLIT-SKIN GRAFTS IN BURNS

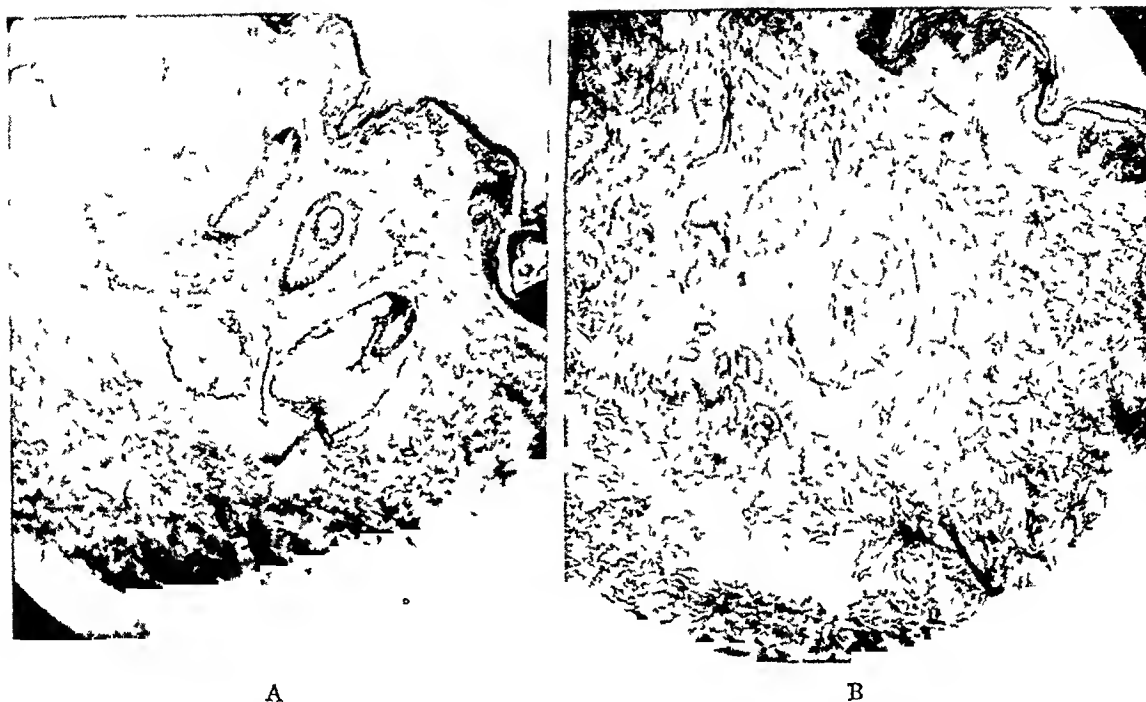


FIG 5—(A) Thick split graft of about three fourths of the full thickness of the skin. (B) Full thickness of the same skin—same magnification. (Ollier Thiersch grafts were supposed to be cut clear up, just under the epidermis.)

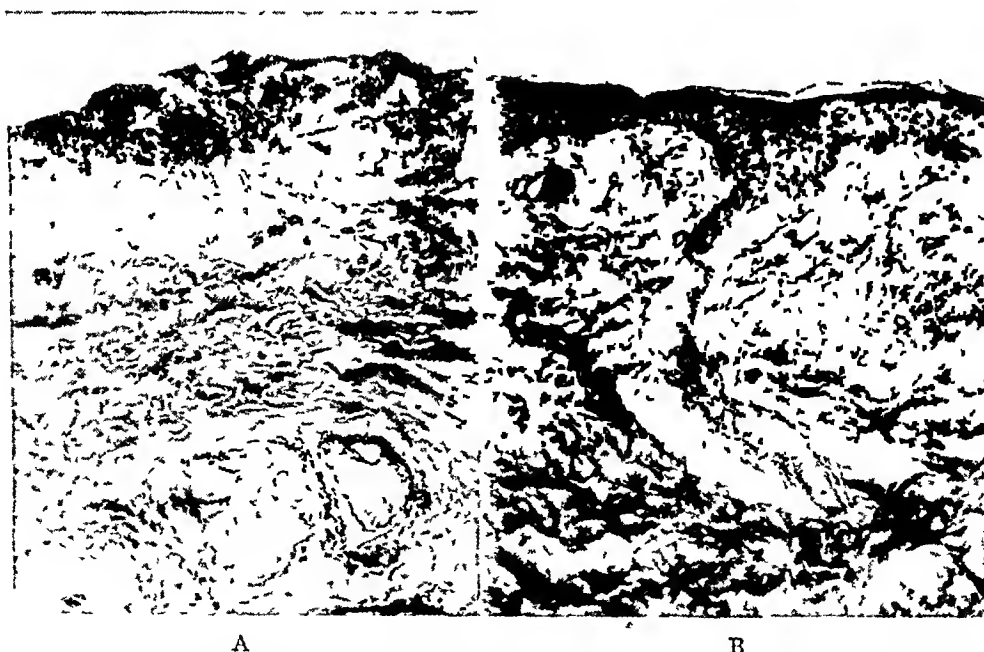


FIG 6—(A) Two day old donor site of thick split graft, with no surface epithelium. (B) Same donor site six days after thick split graft had been removed, showing complete surface coverage, with squamous epithelium, "dedifferentiated" from the deep parts of the hair follicles.

graft was cut just through the papillary layer of the epidermis, which makes it very thin without any derma. However, the pad of derma happens to be a most important part of a skin graft and to avoid confusion, the term "thick split-graft" seems most descriptive (Fig 5)

When large areas are to be covered, it is necessary to obtain large thick grafts without cutting entirely through the derma, so that healing of the donor site can occur rapidly, without leaving any further defect. The deep glands

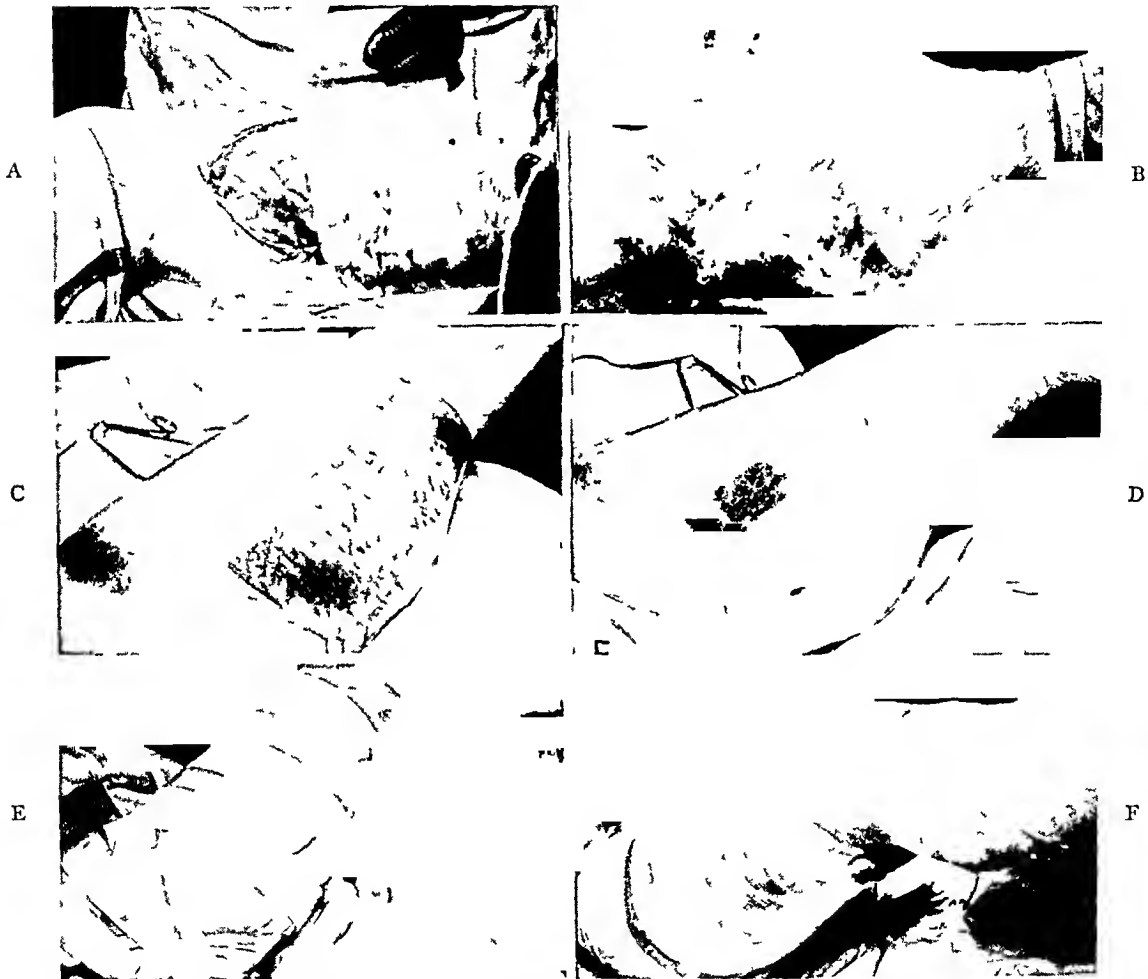


FIG 7—(A) Fine mesh roller bandage of 4 per cent sulfanilamide in an aquaphor like base. Split graft sewed on, overlapping the edges and matted over surface. (B) Cotton mechanic's waste as a medium of pressure. (C) Donor site of thick split graft, with derma intact. (D) Fine mesh scarlet red gauze just over the defect. (E) Donor site carefully protected from mechanical, bacterial and chemical trauma. (F) Whole leg, with firm pressure dressing and joints immobilized.

left behind in the derma of the donor site "dedifferentiate" into squamous epithelium, and cover the surface in from six to eight days. This is shown, microscopically, in Figure 6. It is an interesting study in wound healing and is comparable to the healing of superficial burns. It is probable that this healing occurs from the hair follicles exclusively.

There must be careful protection of the donor sites, and these are dressed with fine-mesh 5 per cent scarlet red ointment gauze, or other suitable oint-

ment, and are supported carefully with adhesive to avoid mechanical, bacterial and chemical trauma (Fig 7) The dressing becomes soaked with serum, but is left on from 10–12 days, at which time it should come away and complete healing have occurred In excessively large removals this added loss should be taken into consideration and whole blood transfusions are often required If the graft has been cut through the derma, or if chemical, bacterial or mechanical trauma has occurred, many new epithelial cells are killed and healing is delayed from three to ten weeks This is comparable to an infected tannic acid membrane on a superficial burn

Cutting Thick Split-Skin Grafts—The most necessary equipment is a very sharp long knife of the amputation variety Large grafts may be cut rapidly, and the larger they are, the more easily they may be applied, grafts up to 5x18 inches may be obtained from suitable thighs, even longer ones can be obtained from some patients (Figs 3 and 4) With some practice, the thickness can be easily graduated with free hand-cutting, and the thickness of the graft should depend on the relative full-thickness of the skin of the area This thickness varies greatly in different parts of the body and in different patients, so that a set-thickness cannot be described for this graft The essential thing is that it be cut thick, but not too thick, to prevent the donor site from healing promptly

The derma of the skin of the back is much thicker than anywhere else, and for this reason, it is one of the best sources Grafts for most raw surfaces, taken from the back, do not have to be cut over one-fourth to one-half the thickness of the skin, and by being careful, as many as five “crops” have been obtained from the same donor area when free-hand cutting has been done, and a second “crop” has been taken as early as 19 days after a previous one Thick dermatome grafts do not permit this

With mechanical aids, such as the dermatome, the suction retractor, or by elevation of the skin with large tenacula, fairly large grafts may be cut, even from the abdomen, but care has to be exercised not to cut through the derma The dermatome may be an advantage for one who is not used to removing split-grafts free-hand, and in children when the thick skin of the back is available The free-hand method is the fastest method, and any time saved is often a great advantage

Application of Thick Split-Skin Grafts—These grafts are applied to the prepared area, and held at about normal skin tension with No 000 silk sutures all around and with multiple mattressing sutures over the surface In suitable areas, the grafts may be spread out and then “snubbed” in place with a sterile fine-mesh roller bandage (Figs 1 and 7)

If the granulations are new, flat, not edematous, and are otherwise bright red and healthy, the graft may be placed right on them It is usually better to carefully shave the granulations down to a smooth, yellow base with a large sharp knife and then apply the grafts The granulations are *never scraped* away If cutting them over a large area will cause too much blood loss, it is

omitted. It is probable that a light dusting of sulfanilamide over the wound before the graft is applied is worth while, and it apparently does not hinder the growth of the graft.

Pressure Dressings on Grafts—A single layer of fine-mesh gauze with 4 per cent sulfanilamide ointment, or other suitable greased gauze (merthiolate,



FIG 8—(A) Open surgical drainage as primary treatment of deep burns. Saline bath and fine mesh gauze dressings as outlined. (Saline low in tub for picture). (B) Total loss of skin from thighs. (C) Restoration left, one operation, with thick split graft, requiring general anesthesia. Restoration right one operation with small deep grafts, with local anesthesia. This leg was six months behind the left one in final recovery.

4 per cent xeroform, or scarlet red) is placed smoothly over the graft and pressure is obtained over the area with mechanic's cotton waste, bound on firmly with heavy gauze rolls. The application of pressure to the dressings is a fundamental, and as important as any other operative step. This cotton mechanic's waste can almost entirely replace marine sponges as a medium

of pressure, it is better in most places, and is a great deal cheaper. A good grade is used, and is obtained from plumber supply sources, as none of the gauze companies prepare it (If contamination is thought to be marked, a wet pressure dressing can be used) (Figs 1 and 7)

Subsequent Care of the Graft—If satisfactory, the dressing is to remain from four to six days. It can then be changed, the sutures removed, and the excess edges trimmed away. If the area is clean, the same type of dressing is reapplied and then changed as necessary. Blebs are trimmed away, hematomata are opened and, if there is infection, sulfanilamide applied locally, and wet (but firm pressure) dressings are applied and changed each day. Later on the greased gauze resumed.

Full-thickness grafts are not placed over large raw surfaces because the size required is prohibitive, and the "take" of a full-thickness dissected graft is not as certain in contaminated fields as that of the split-graft. This graft is used in late deformities, especially for areas not covered by clothing. For this reason, it is important to save a donor site on badly burned patients, if possible, so that smooth full-thickness grafts may be obtained when final operations are to be undertaken about the face and neck.

HOMOGRAFTS AS EMERGENCY "DRESSING" FOR WOUNDS

It may be a life-saving process to go to the trouble of applying large sheets of split-homografts in patients who cannot stand a long operative procedure, and who are "slipping" daily from debilitation and pain. Homografts take almost as well as autografts, and survive from three to ten weeks. During this period, the patient is given a respite from pain and dressings, his general condition picks up, and there is a stimulus to his own epithelization, so that complete healing even may occur after absorption of the grafts. This notable increase in wound healing has caused some observers to think that homografts survive permanently. The grafts absorb in a rather clean fashion, just fading away from the third week on, without infection usually, and leaving a clean granulating base (Fig 2).

There does not seem to be any relation of the "take" of a homograft to the blood group, even though the blood has been grouped down through the M and N groups. If these grafts could be gotten to survive, one of the greatest problems in plastic surgery would be solved (Fig 1). Homografts in identical twins have been shown to survive permanently, experimentally, and if a twin were burned, homografts from the other twin could be used, with a good chance of their surviving.

Early grafting of burns and other wounds—It is assumed that most observers believe that the earliest possible grafting of open wounds is advisable and that the primary excision and grafting of burns may be applicable occasionally.

Repairs of Contractions—The repair of fresh wounds that have not had time to contract cannot be completely separated from those that have con-



FIG 9—(A) Unhealed burn after several months with dirty, crusty wounds, and consequent intractable pain. Dirty, inadequate coarse mesh gauze dressing. (B) Cleaned up. Grafting of raw areas first, to control pain and infection. Later corrections with more free skin grafts.



FIG 10—(A) Contracted axilla opened because of a dirty sinus, deep in the scar. (B) Total restoration of function having persisted through an 11 year growing period—221 square inches of thick split grafts transferred to cover chest, back, arm and entire axillary region. Two graft operations.

tracted, as this, of course, depends on when the patient is first seen or how soon he can stand operation. The open wound requires just grafting, while the contracted one requires relaxation and restoration of parts of their normal positions. Sometimes, of course, both have to be done, but if there is an open, dirty wound over part of an area, and a flexion deformity along with it, it is often best to obtain healing first by grafting the open area and considering the deformity later, rather than opening into a clean flexion area through a dirty surface, or a dirty sinus may be opened and cleaned up before any grafting is attempted (Figs 4, 9 and 10)

The patients illustrated are not so much case reports, as to show examples of the various points listed in the paper. Long histories and details are omitted because the original premise is thought to be true—that these repairs of massive burns can be undertaken successfully and in a fairly acceptable routine manner, and that the laborious use of full-thickness grafts and pedicle-flaps can be avoided in many instances.

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DISCUSSION—DR JOHN STAIGE DAVIS (Baltimore, Md) This paper of Doctor Brown's has been exceedingly interesting, and the extraordinarily fine results we have seen illustrated are excellent. To cover these enormous burns with great surfaces denuded of skin, a number of large thick split-grafts, equaling the defect in size, can be cut and sewed together, or applied singly. It must be realized, however, that when that amount of graft is taken from the surface of the skin, one is doubling the size of the denudation of the skin surface. The grafts act as a dressing only, for a period of a few hours until healing begins.

I would like to ask Doctor Brown whether the great increase in the size of the denuded area caused by cutting these large grafts has had any upsetting effect on the patient

DR WALTMAN WALTERS (Rochester, Minn) Would it be possible for Doctor Brown to speak a little about the management of these cases, for the benefit of those of us who do not know so much about plastic surgery If he could do this I believe it would be very welcome

TRENDS IN SURGERY

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THE HUMAN RACE has through the ages looked for some panacea which would bring relief for all its ills. This applies most particularly to physical defects, deformities and disease. Each age found its best savants and students so engaged.

The earlier advances were very slow—the result of the difficulties of transportation and the lack of contacts. Century after century passed, each adding but limited knowledge. Its gradual growth was more or less constant. Always the search began with matter, its formation, its elements and their changes, which were most impressive not only to the early investigators but continue until this day. Each individual searched in the particular field which most impressed him. To see the mind of a child unfold even at present is remarkable, and the difference in the alertness, the quickness of perception and tenacity of memory in some children as compared with the dulness, slow perception and inability to grasp ideas in others, at once brings the question of why this is true. So in adults every mind will produce better results if directed in its natural bent. The psychologists have long recognized this fact. Every man who handles large groups of individuals notes and employs this idea to get the best results.

First, in the order of development, came the effort to obtain physical comfort. Food was necessary to sustain life and the search for it is noted in every form of organism from the lowest and smallest to the largest and most complicated.

Every outside influence upon life processes naturally impressed the individual. The materials contacted brought matter to his attention. Land, sea, and the simpler elements, water, air, fire, and the physical change in their form and structure excited the curiosity of man. Light and darkness, heat and cold, each brought wonder and the desire for knowledge to the active brain. It is not possible that all these things were taken by everyone as a matter of course. There were bound to be some who desired an explanation of these phenomena.

The contest with the elements resulted in the formation of communities for defense and protection. It is not remarkable how slow was the increase in knowledge but how wonderful and gradual was its development. It is the general belief that facts reach the individual and the community when they are prepared to receive the information.

This discourse is held to call your attention to medical progress through

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the era of mythology and tradition, mysticism and fact, the darkness and confusion of the middle ages, the progress and illumination of the later days, the errors in reasoning and conclusions in many instances, and the manner in which each increase in learning unfolds. Much stumbling occurred in every branch of science, but this brought, in every age, demonstration and proof of the correctness of certain ideas.

We desire only to mention the early writers on medicine, alchemy, chemistry, anatomy, physiology and histology, to make you realize just how much we owe to these investigators.

"Reading maketh a full man, conference a ready man, and writing an exact man." Could one realize the increase in knowledge contributed by each generation as time progresses, the result would be surprising. Excursions through the literature always bring to the reader an admiration for the early investigators. Our study here of the early years must naturally be sketchy and only mentioned to call your attention to the outstanding facts established as the final result. Much of the knowledge has been obtained by accident after prolonged hours of study. The description given by Kekulé of how the benzene ring came before his consciousness in a half dream state after a long conference with his friend, Mueller, and of its later confirmation in the light of cold reason, is illuminating. The same is true of the accidental discovery by Sir William Ramsay of the beautiful mauve color which resulted when he was about to throw into the discard an ugly, muddy material at the end of a day's work, but decided to pour alcohol into the flask when suddenly the beautiful color appeared. From this incident came the aniline dyes and the many chemical combinations including the sulfonamide group so valuable in pneumonia and other infections.

In my search of the literature it has been necessary to quote freely from *The Doctor in History*, by Howard W. Haggard, Yale University Press, 1934. I have received much information and wish to give the author and the publishers my thanks for the permission. Credit must be given also to Dr. Henry E. Sigerist, the editor of *American Medicine*, and to its publisher, Yale University Press, 1934. In the first paragraph of his preface Haggard says "Daudet, presumably with a view to their moral sophistication, wrote Sapho for his children to read when they were twenty-one. Chesterfield wrote his letters in the interest of his son's social elegance. I know nothing of the effect on Daudet's children, Chesterfield's son did not appear to benefit. Nevertheless, hopeful, as parents will be, I have followed the example and written this book for my children. Not, let me hasten to say, for their morals or their manners. Perhaps it is a reflection of changing times, or possibly merely of my own interests, that I am frankly concerned less with these matters than I am with some other aspects of their education and their health—especially their health. What I have tried to write for them is a history of health."

Credit must be given to the many writers and historians for what occurred in early Egyptian and Greek medicine. The very early stories are surrounded

by uncertainty and are full of legendary and at times improbable statements. Therefore, they have largely been omitted and we have attempted to include only written statements which have the semblance of truth.

It is not surprising that in the early years for a number of centuries the Church was closely involved with medicine because it was far advanced in education and interested in human welfare. For a time the clerics practically controlled the practice of medicine.

As superstition lessened under advancing knowledge religion increased in power and the prelates of the Church were the foremost students of that period. It was the natural function of the Church to succor the sick and care for the indigent. Hence, men interested in medicine and in surgery sought knowledge where it was most advanced. The early Egyptians were learned in medical lore, and from Arabia and Persia came rumors of wealth and wonderful cures of disease, finally reaching Greece and Rome. The conditions led to attempts by one country to overcome another and to obtain its wealth and its knowledge. Then wars brought more information and developed in addition to medical lore the necessary knowledge of surgery to care for the injured soldiers. Epidemics and plagues resulted, giving a stimulus to medical search for prevention and cure. The names so engaged are legion. Credit is given to Hippocrates, of Cos, for bringing medicine from speculation and superstition to the realm of fact. He not only contributed to the history and symptoms of disease, but recorded the history of his cases and gave methods for operation upon surgical lesions. In his writings he describes the Hippocratic facies, so well known to all practitioners. Naturally he was not so positive as Galen and others who had more facts to guide them. The value of recording symptoms, the time of their appearance, and the changes occurring with the methods of treatment first came into use, and to-day the value of the history of the patient is recognized. It has become well established in the recognition of a hospital as meeting the requirements for the instruction of interns, house physicians and surgeons.

"Hippocrates with his honesty, his insistence upon clear reasoning, and upon observation of facts, rather than speculation expresses the ideal of our modern medicine. In the early years studies in anatomy were not easy of access because of prejudice against disturbing the dead, particularly in Egypt, and cadavers could not be obtained. Occasionally skeletons were found for the study of osteology. The Greek army after the death of Philip, of Macedon, under the command of his son, Alexander the Great, completed the conquest of Persia and the whole Eastern world as far as India." He founded the city of Alexandria and placed the first Ptolemy as its ruler. "With the army went scientists to collect information from every country for Aristotle's great books on natural history." A great museum and library were erected at Alexandria, and a vast number of manuscripts of Greek scholars were collected. Alexandria became famous as the great seat of learning in all branches of study including medicine. "People came from every part of the world, beliefs were mingled, old religions were discarded and new ones grew up."

Here Herophilus made dissections of animals and wrote a textbook of anatomy which was really a scroll, a hand-written manuscript. Following the conquest of Alexandria by the Persians under Cambyses, Imhotep, with a reputation increasing for 2,000 years after his death, had become a god—the Egyptian God of Healing and Medicine. “The temples where he was worshipped were in a way hospitals and were schools of medicine and magic.” “These priests wrote on papyrus of the diseases they saw and the treatment they gave.” “These temple papyi were the first written records of medicine—the first medical books.” “The Greeks were open minded, respected the gods of all people but gave none a profound reverence.” “When at length their sailors and merchants came to Egypt, they saw in Imhotep not a rival deity but their own God under a different name. They called him Imuthes and linked his name with their own God of Healing, Æsculapius.” According to Haggard, “Egypt had reached the peak of its civilization and was declining, dying.” Its art, its architecture, its literature, had become formal—unchanging.

“But this country of tombs and mummies became with the passage of centuries a vast storehouse of wisdom from which other and younger civilizations, more progressive, were to learn something of the mysteries of life and death, of health and disease.”

The Anatomic Era began with Herophilus (335–280 B C) and continued to the time of John Hunter (1728–1793 A D), during the greater part of this time but little progress was made in anatomic studies because of the difficulty in obtaining dissecting material. This limited the number of students of anatomy. It was not until the 16th century that Andreas Vesalius wrote the first true human anatomy, based on actual dissections, yet all the teachers of anatomy said that it could not be correct because it differed from Galen. Some went out of their way to irritate and embarrass him. He became so indignant that he burned his manuscript, quit anatomy, left Padua, and became physician to Emperor Charles V. While isolated at the court some mild inquiries were made to see if he were correct, and it was found that he was. Vesalius was soon forgotten, a fact which caused great disappointment in his life, entirely undeserved, yet not so tragic as the treatment accorded Ignatz Philipp Semmelweis in Vienna.

For years physicians in England and in France took the position that it was beneath their dignity to be asked to do any of the menial work in the care of the sick. Their attitude was that their superior knowledge of disease, and their diagnostic acumen, placed them in a class by themselves. Their College of Physicians would not permit a barber surgeon or surgeon to be elected to membership. “The physicians looked with contempt upon surgeons, few educated men cared to take up this branch of medical study.” “The lack of knowledge of Latin, because they had not studied in the University, placed them as surgeons of the short robe.” Paré, who accomplished some remarkable feats in surgery, belonged to this group. He was one of the first to combat the idea that the surgeon was a menial and inferior to the physician.

In 1536 Paré went with Marshal Montejan as his regimental surgeon. "I was at that time," says Paré, "an untutored soldier, I had not yet seen wounds made by gunshot at the first dressing. It is true that I had read in Jean De Vigo that wounds made by firearms were poisoned wounds, because of the powder, and for their cure he commanded to cauterize them with oil of elder, scalding hot, in which should be mixed a little theriac, knowing that such a thing would bring great pain to the patient, I wished to know first how the other surgeons did for the first dressing, of whom I took courage to do as they did. At last my oil lacked, and I was constrained to apply in its place a digestive made of the yolk of eggs, oil of roses, and turpentine. That night I could not sleep at my ease, fearing that by lack of cauterization I should find the wounded, upon whom I had failed to put the oil, dead or poisoned, which made me arise early to visit them, where beyond my hope I found those upon whom I had not put the oil feeling little pain, their wounds without inflammation or swelling, having rested fairly well throughout the night, the others, to whom I had applied the boiling oil, I found feverish, with great pain and swelling about their wounds. Then I resolved, with myself, never more to burn thus cruelly poor men wounded with gunshot."

Paré was a born surgeon, with a temperament suited to his calling. As shown in the above narrative told by himself, he had the milk of human kindness in his soul and a desire to serve. He followed the leaders as far as his judgment permitted but did not hesitate to change his plan of treatment when the need arose. A surgeon never soars to great heights when bound by a rule of thumb. He always remains an imitator and not a master of his art.

Paré had surgical instincts and rare judgment, he restored the use of the ligature to control hemorrhage, which had been used centuries before by the Romans but was discontinued. By this method secondary hemorrhage was less frequent than from the cautery or boiling oil, and it is the safest method for this purpose today.

William Harvey (1578-1657), a graduate of Cambridge, went to Padua and received his Doctorate in Medicine in 1602. He made a calculation, in 1618, that two ounces of blood passed through the heart with each beat "72x2 ounces, 144 ounces a minute, 540 pounds an hour." "Absurd to think that the body produced that much blood. There could be only one answer, the blood circulated." In the seventeenth century came the first transfusion of blood, and considerable debate occurred as to what would happen to the character of the recipient. At present more interest is taken in the immediate result to the reaction, and the incompatibility. In those early days there was no knowledge of microbic infection with suppurative organisms, nor was lues, the serious social evil, then discussed publicly in the forum or drawing room. Men said that Harvey was wrong because Galen found it otherwise. On the other hand, Servetus called attention to Galen's mistake in this matter, pointing out what he thought errors in religion, a very unwise thing to do. "Servetus was burned to death in 1553." The work of Harvey, and the two Hunters somewhat later, determined opinion on surgery of the

blood vessels and opened a wide field in every portion of the body. The reparative power of the blood vessels is not surpassed by any structure, not even the peritoneum nor the lung. Stab wounds of the heart closed by suture have been known to heal completely within 17 hours, the patient dying of a concurrent injury. One by one every field of the body has come within the reach of surgery of to-day. The abdominal aorta has been opened in planned operations a number of times, not often with success but enough to demonstrate its possibility. Death may occur from other emboli and the wound in the aorta is found healed. Embolectomy of smaller vessels has been successful. Sutures of arteries, in their continuity, after traumatic rupture have been safely completed after repeated failures, as was the case in the first vesicovaginal fistula which made James Marion Sims famous. The best men in all ages have failed, and so reported, but continued their efforts until their task was successful. Clots were removed from arteries in their course, both from peripheral and pulmonary vessels with a diminishing mortality. Matas, by his aneurysmorrhaphy, in 1888, systematized it in 1902 thus he made a great contribution to the surgery of the vessels. By this operation it was hoped to restore the circulation without impairment of the nourishment of the limb.

The studies of Pasteur, Koch, Behring and others of microbes and their place in fermentation and suppuration opened a new line of thought. The views expressed by the bacteriologists that minute living organisms caused both fermentation and suppuration in wounds were not at once accepted. It was my good fortune, immediately upon graduation, to hear the debate on each side of this question. Joseph Lister was one of the first to accept this view as a fact and no longer a theory. He claimed that the only way to overcome this contamination was by the use of carbolic spray about the wound and in the air of the room. The hands of the surgeon and all of his assistants, with all others coming into contact with anything used in the operation, were placed in dilute carbolic solution after being thoroughly scrubbed. His paper was published in 1867, and during the next decade he gained considerable reputation and was knighted. His antiseptic method worked well but required too much paraphernalia. Mr. Lawson Tait soon proved that equally good results could be obtained by simple kitchen cleanliness. This method was promptly adopted by the whole medical profession. The proof of the correctness of the view that pus production in wounds resulted from bacteria was so apparent that the debate here rested on the question of whether the views of Lister or of Tait would prevail. Gerster's book came to my attention, and the younger men followed and accepted the idea that this was no longer a theory but a fact. We soon became converted to Tait's view of asepsis and found the results to be satisfactory.

Then American surgeons took the lead and made many new advances in technic, employing rubber gloves, and covering the head and face with a cotton hood, and showed fine records in new fields. There were some changes in operative methods and the preparation of the field from time to time. Soap, water and alcohol made preparation of the wound simple and satisfactory. It

was found in several clinics that too much scrubbing diminished the resistance of the skin, and this was given more care and less energy, because soap and water made the preparation too "sloppy" and at times left the patient wet, the trend simultaneously throughout the country was to employ a 3 5 per cent iodine solution. This method was time-saving and left the field dry, and was in vogue for a considerable time. Because of a few cases in children where the solution was too strong—producing blisters—70 per cent alcohol was substituted, with success. At the present time most clinics have adopted alcoholic solution of merthiolate for this purpose. During this period the progress in surgery in this country was remarkable.

On my first trip abroad, in 1900, Sir William Macewen, whom I consider one of the best surgeons of my acquaintance, used the same technic then in use here. In Edinburgh, a few hundred miles away, the contrast with the technic in the clinic of Sir John Anandale was noticeable. The latter was a fine surgeon, of the old school who had not yet adopted the new methods. Macewen and Sir Victor Horsley, in London, using the same technic, were opening up cerebral surgery and by their observations were contributing much to the knowledge of the physiology of the brain.

On the continent I found the same high-grade type of work in Berlin, where Dr. Theodore Kocher was undertaking the largest and most successful surgery on goiter, and it was a pleasure to watch him work. He used many silk ligatures in the neck, which I have never found it necessary to employ, but his results were excellent. There are some surgeons here who seem to be drifting back to the use of silk sutures instead of catgut, which has always served me so well. They may be correct but my experience makes it doubtful, and I should advise a change in the make of catgut, which will probably remove any objections they may have to its use for sutures or ligatures. There will probably be a number of minor changes in technic from time to time, but, in the main, the general trend is toward uniformity in practice, especially in this field, which has become greatly enlarged within recent years.

The greatest changes have occurred since 1900, when I found Macewen and Victor Horsley opening up new fields in cerebral surgery, and these changes have been remarkable. Notwithstanding the fact that a number of medical men of ability claimed that further advance would be only in the field of technic, it has been disproven by the increased knowledge of function in the different portions of the brain, and by the remarkable results in the treatment of tuberculosis. Moreover, it is true that a great increase in our knowledge of pulmonary diseases is the result of marked improvement in methods of roentgenologic examination. It appears that the progress continues about the same in every field of medicine.

A remarkable change followed the communication of Oliver Wendell Holmes on the contagiousness of puerperal fever, in which he made the statement that this disease was the result of microbic poison carried to the patient in childbirth. This contention was also made a little later, most vigorously, by Semmelweis, in Vienna. He so offended the obstetricians that he was

driven from Vienna, but in Budapest produced positive proof that he and Holmes were both correct. This was the most remarkable advance in obstetrics in a century.

The Dean of Gynecologic Surgery in the United States, Dr. Howard A. Kelly, contributed perhaps more than any other man to this field, and to surgery of the pelvic organs and the urinary tract. Kelly must be given due praise for the patience and persistence with which he worked for the methods of cystoscopy and ureteral catheterization. In addition to a very large surgical and gynecologic practice, he gave an immense amount of time to improvement of technical methods of operations in the pelvis and perineum. He has written the most valuable and elaborate treatises, beautifully illustrated by Max Brodel, and others, and acquired a wide reputation. In this work he was ably assisted by Thomas S. Cullen, Guy L. Hunter, Curtis F. Burnam, and other members of his staff. Doctor Kelly was the first American to recognize the value of the discovery of radium by Curie, with its wonderful possibilities, which, with the use of high-voltage roentgen rays, covers a large field in the treatment of skin, glandular diseases, and types of malignancy. It is often very effective.

One of the most important developments, and aids to both medicine and surgery, came when William Crookes, an English physicist, brought out the vacuum tube. It was looked upon as a useful means of instruction for students of electricity, and few could visualize its possibilities. The observations of Wilhelm Konrad Roentgen, in 1895, that "a piece of paper coated with certain metallic salts held in the light from a Crookes's tube the coating glowed with a curious phosphorescence." The glow continued when the paper was removed from the tube. "He held a piece of metal before the paper, a shadow was cast, he held his hand before it and saw what no one had ever seen before—the shadow of the bones of his hand." These rays affected photographic film, and pictures could be made of structures beneath the skin. These observations created a furor. Its practical use was not evaluated. The determination of lines of fracture and of the presence of foreign bodies in the esophagus, the trachea, lung and the gastro-intestinal tract and, subsequently, vesical stone, was a marked step forward.

Then it was that the impetuous operator of the roentgenologic department, in spite of Roentgen's advice that red lead paint be used to protect the operator against the rays, learned of the danger of burns from this source. Quite a number developed troublesome ulcers and these vascular disturbances became cancers. Sometimes the hero dies because of his search for knowledge, and his love of humanity. Coolidge and the radiation tube opened a vast territory for the benefit of mankind.

Stones in the gallbladder were soon found interesting, but only a small proportion were shown by the early technic. Graham and Cole by the use of dyes opened a still newer field in the determination of the function of the gallbladder and increased our knowledge. During these years of study, gastroenterology was clarified by the use of bismuth, and later barium, to visualize

these structures The work in osteology continued, and with the dyes, a Bucky diaphragm, and intravenous injection of diadast and uroselectin, renal lesions became an open book, including the ureter throughout its course, and the bladder This recalls to my mind how we had to make a diagnosis of hydronephrosis, tuberculosis of the kidney and tumor, without such valuable aids Cephalography with an injection is a remarkable development and tells much to the cerebral surgeon The trachea and the lungs have been longer under observation But now the newer technic can isolate and outline to the most minute detail the size, content and location of a pulmonary cavity, an abscess or a growth Body section by roentgenography, laminography and tomography solves many problems for the physician and the patient, previously obscure

The specialist in roentgenology will tell of three methods of body roentgenography

- (1) Focal spot of the tube moves in one direction in a straight line
- (2) Focal spot of the tube crosses circles, squares, or archimedean spirals, but remains in plane of film
- (3) The focal spot of the tube and film rotates about an axis moving in parallel lines

The study of the spine, the pelvis, with pelvimetry for deformity, and the relative size of the structures and the head of the child tells the obstetrician much about what steps he must take for safe delivery, and the best time

The human frame has become an open book under the advanced study of every part of the patient's anatomy, the specialists and the family physician each giving his best to place the treatment on a correct basis for cure while it is yet possible How could such scientific progress result except by the individual and competitive system?

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THE UNIFORM PRODUCTION OF EXPERIMENTAL SHOCK BY CRUSH INJURY POSSIBLE RELATIONSHIP TO CLINICAL CRUSH SYNDROME

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IN RECENT MONTHS a number of clinical reports^{1, 2, 3, 4 5} have appeared on the condition which results from the compression of extremities by heavy objects for periods of several hours or longer. Most of these accidents have occurred in association with air raids in which persons have been pinned beneath fallen debris. The essential clinical features are these. The patient is usually in fairly good condition at the time of release of the compression, evidences of shock generally develop within a few hours, the immediate response to therapy is usually favorable, and subsequently, after a period of hours or days, the patient develops signs of progressive renal damage. The urinary output diminishes at this time, there is nitrogenous retention, and the urine contains albumin and large orange or brown granular casts. In approximately half of the reported cases death occurred in three to eight days following the compression.

The present study was undertaken in an attempt to reproduce experimentally the so-called crush syndrome. The first efforts consisted in compressing the extremity of the experimental animal by various means, including the use of tourniquets, encircling layers of rubber dam, and pressure between two smooth boards. The results which followed the use of these methods showed considerable variation. It then appeared to be advisable to use objects for compression which did not have a smooth surface and which would exert an uneven pressure, resulting in greater injury to tissues. This method, which will be described in detail, has resulted, in our hands, in the more uniform production of peripheral circulatory failure than we have been able to accomplish by other procedures.

It cannot be stated with certainty that our method has resulted in the causation of the so-called crush syndrome, in fact, it has not been proved conclusively that the crush syndrome as observed in patients is a distinct clinical entity, with features which may not be found following other types of injury. Regardless of whether or not the crush syndrome has been reproduced, the present studies have yielded what appears to be a rather uniform method of causing shock, in which an increase in the concentration of the blood and a fall in blood pressure occur early following the release of the compression.

The present communication presents a description of the method, a report of the effects of compression of one of the posterior extremities of the

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anesthetized animal, and the results of attempts to influence the course of the animals following the release of the compression

EXPERIMENTAL METHOD

The experiments were performed upon dogs weighing between 7 and 11 Kg. Morphine sulphate in doses of 0.30 Gm. was given subcutaneously at the beginning of the experiments. Approximately 30 minutes later sodium pentobarbital, 0.20 Gm. per Kg. of body weight, was given intravenously. One or two subsequent doses of 0.06 Gm. per Kg. of body weight were usually necessary to maintain anesthesia during the following 18 to 24 hours. The mean arterial blood pressure was determined repeatedly by direct needle puncture of the femoral artery. Hematocrit readings were made with Wintrobe tubes. The bladder was catheterized at the beginning of the experiment and the catheter left in place, so that the character and volume of the urine could be observed at one- to two-hour intervals. Nonprotein nitrogen, plasma creatine, and plasma creatinine levels were determined by the method of Folin and Wu.⁶ Blood samples were taken at the beginning of the experiment, immediately before the compression of the limb was released, at one hour, four hours, and six hours subsequently. Creatine and creatinine levels in the urine were determined at corresponding intervals (on individual specimens) by the methods of Folin.⁷ All colorimetric determinations were made with an Evelyn photo-electric colorimeter. Urine samples were examined at the beginning of the experiment, and every one to two hours thereafter during the experiment, as to volume, gross appearance, presence or absence of albumin, benzidine reaction, hydrogen ion concentration (litmus), and microscopic appearance.

Compression of a limb was produced by an apparatus (Fig. 1) consisting of two three-quarter-inch boards, 15 inches long and seven inches wide, on the inner surface of which were fixed triangular strips of wood measuring $1\frac{1}{2} \times 1\frac{1}{2} \times 2\frac{1}{4}$ inches. These strips were placed so that when the boards were approximated their coaptation resulted in a cog or gear-like arrangement. In the center of each strip a groove, one inch in diameter and three-quarters of an inch deep, was made corresponding to the course of the femur. This groove prevented interference with the approximation of the strips and thus ensured the crushing of a larger mass of muscle. Holes, which were three-quarters of an inch in diameter, were drilled in the four corners of the boards. Into these were inserted one-half-inch iron bolts, which were 11 inches long. Threads extended half the length of the shaft and these were fitted with large wing-tipped nuts. Steel compression springs, four inches long, fifteen-sixteenths of an inch in diameter, one-eighth of an inch wire diameter, with 13 effective coils, were placed on the bolts on the upper board. Suitable steel washers were used to protect boards and springs. The springs were calibrated by placing them between the boards and measuring the millimeters of shortening produced by a weight of 500 pounds, which was placed on the upper board.

The dog's thigh was placed in this press and a pressure of 500 pounds was applied for a period of five hours, at the end of which time the press was removed. Approximately half the animals were given no treatment after release of the compression, and observations were made at the intervals de-

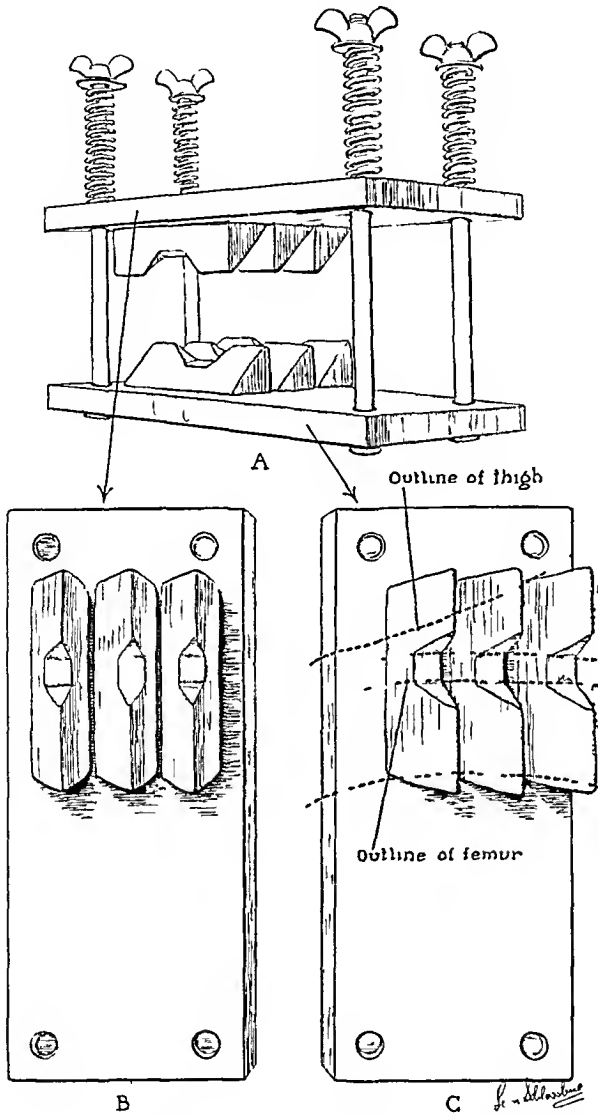


FIG. 1—Drawings of apparatus used for limb compression. (A) Side view of assembled apparatus with upper board elevated to show relative position of its parts. Pressure is applied to the upper board by tightening the wing-tipped nuts and shortening the springs. (B) Apparatus taken apart to show position of triangular strips of wood and the groove in their centers to fit the approximate course of the femur. These strips are so arranged that their apices fit into the spaces between the strips of the opposite board. In other words, the sharp edges are so placed that they do not touch each other but fit into the corresponding spaces.

scribed above. The other half were treated by the application of a pneumatic rubber cuff (Fig. 2) which was applied to the injured extremity immediately upon release of compression. This cuff consisted of an outer layer of thick rubber which was cylindrical in shape, 17 inches long and five inches in diameter, and an inner layer of thinner rubber which was conical in shape.

PRODUCTION OF SHOCK BY CRUSH INJURY

in order to fit the contour of the extremity snugly. The cuff was fitted with a valve which was connected to the compressed air supply. A mercury column valve was interposed to ensure constant pressure. By means of this cuff a pressure of 40 Mm Hg was applied to the extremity for periods of 13 hours in some experiments and 18 hours in others. The loss of fluid into and near the injured area of the animals which died was determined by a bisection method that was described previously.⁸

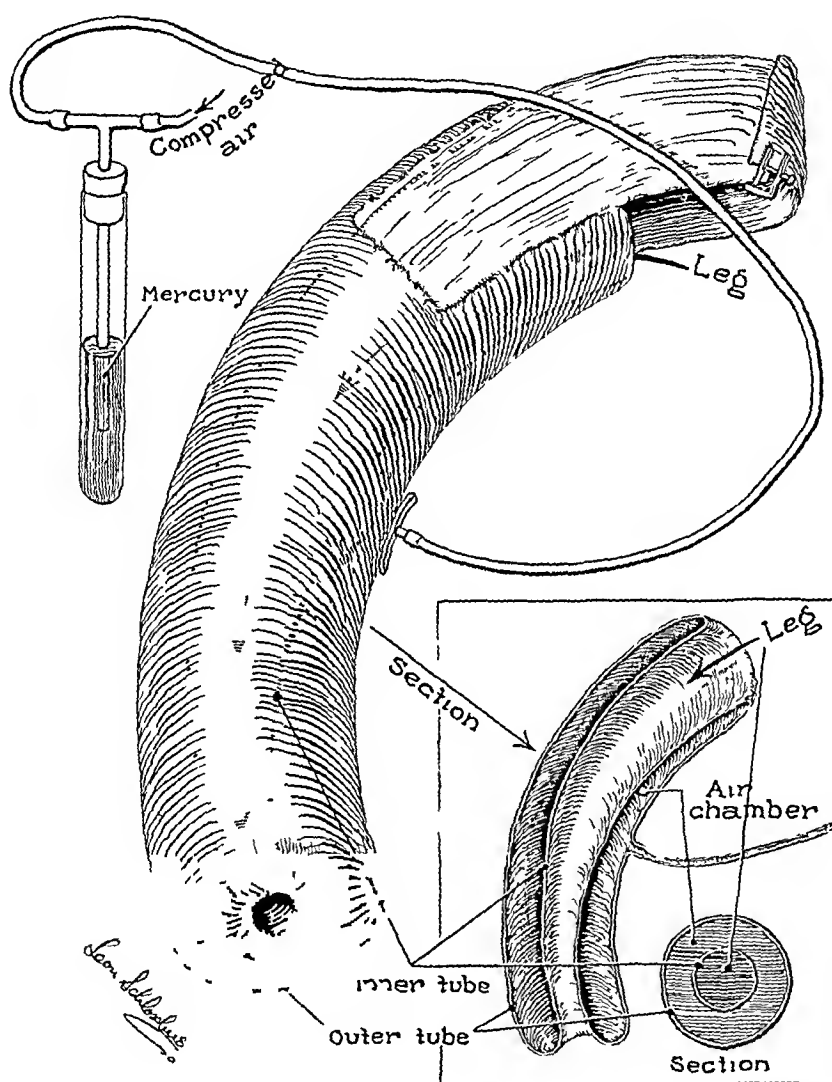


FIG. 2—Drawing of the pneumatic cuff used in treatment of crushed extremities. The rubber strips at the upper end of the cuff encircle the animal's lower abdomen and are held together by a screw-clamp. Insert—Longitudinal section of the cuff showing air space and conical shape of inner tube which is in contact with the extremity.

RESULTS

The results are summarized in Tables I, II and III. For purposes of description the results of the experiments will be divided into (1) Crush period, or period of five hours of compression of the extremity, (2) the period following release of compression, no therapy being employed (half of experiments), and (3) the period following release of compression, pressure therapy being used (half of experiments).

TABLE I
THE EFFECTS OF CRUSH INJURIES (UNTREATED GROUP)

Mean Blood Pressure Mm Hg			Pulse Rate per Min			Hematocrit Reading			Respiratory Rate per Min			Temperature Degrees F			Hours Survived After Press Removed	Fluid Loss% Body Weight (Local)
Exper No	Reading 2-6 Hrs After Press Removed		Reading 2-6 Hrs After Press Removed		Reading 2-6 Hrs After Press Removed		Reading 2-6 Hrs After Press Removed		Reading 2-6 Hrs After Press Removed		Reading 2-6 Hrs After Press Removed		Hours Press Applied			
	Control	Press Removed	Control	Press Removed	Control	Press Removed	Control	Press Removed	Control	Press Removed	Control	Press Removed		Control	Press Removed	
1	130	95	120	172	48.2	71.8	8	12	101.4	102.4	5	6	5	6	3.04	
2	130	50	68	200	50.2	72.2	10	6	99.6	99.0	5	16 hrs 15 min	5	16 hrs 15 min	3.39	
3	115	95	56	160	48.3	55.4	6	6	98.9	99.6	5	8	5	8	3.02	
4	125	75	140	200	44.3	64.7	6	12	98.0	98.0	5	12	5	12	3.42	
5	125	100	120	200	39.4	43.4	10	16	99.4	102.1	5	Recovered	5	Recovered		
6	125	50	140	200	42.9	67.5	12	6	98.8	98.0	5	7	5	7		
7	115	115	96	108	40.7	58.0	8	8	99.4	99.4	5	12	5	12	3.97	
8	120	90	84	200	50.4	76.8	10	16	100.0	99.4	5	4 hrs 35 min	5	4 hrs 35 min	3.81	
9	130	45	120	200	51.3	67.0	8	20	99.0	102.2	5	10	5	10	3.40	
10	115	75	140	200	56.0	71.1	10	20	99.4	99.0	5	14	5	14	3.12	
11	125	120	120	160	41.7	72.7	16	16	100.2	98.9	5	6	5	6	2.97	
12	125	70	120		48.4	74.3	6	16	100.1	102.1	5	2 hrs 20 min	5	2 hrs 20 min	2.94	
13	115	85	120	186	55.0	74.0	10	24	101.2	103.6	5	6	5	6	3.46	
14	110	75	100	200	56.6	75.8	6	40	100.1	103.1	5	12	5	12	3.88	
15	130	50	112	200	42.2	72.7	10	40	100.8	103.5	5	2 hrs 15 min	5	2 hrs 15 min	3.51	
16	120	45	172	200	50.4	76.4	10	40	100.9	103.5	5	5 hrs 15 min	5	5 hrs 15 min	3.04	
17	130	60	104	180	53.2	78.0	8	40	99.8	102.6	5	5 hrs 15 min	5	5 hrs 15 min	3.22	
18	125	40	96	172	53.7	72.7	6	10	100.8	102.5	5	11	5	11	2.64	
19	120	88	140	200	42.7	74.0	6	6	100.6	102.4	5	6	5	6	2.67	
Average fall 49.89 Mm Hg			Average rise 72.7 per min			Average rise 44.0% over control values			Average rise 12.00 per min			Average 7.55 hrs (excluding survival)			Aver- age 3.26%	

PRODUCTION OF SHOCK BY CRUSH INJURY

TABLE II
THE EFFECTS OF CRUSH INJURIES AND OF COMPRESSION THERAPY

Exper No	Mean Blood Pressure Mm Hg		Pulse Rate per Min		Hematocrit Reading		Respiratory Rate per Min		Temperature Degrees F		Hours Pneumatic Cuff Applied	Hours Survived After Press Removed*	Fluid Loss% Body Weight (Local)
	Con- trol	Reading 4-6 Hrs After Press Removed	Con- trol	Reading 4-6 Hrs After Press Removed	Con- trol	Reading 4-6 Hrs After Press Removed	Con- trol	Reading 4-6 Hrs After Press Removed	Con- trol	Reading 4-6 Hrs After Press Removed			
20	120	115	152	180	40 8	58 8	6	10	100 8	98 2	13	Recovered	3 12
21	120	105	132	180	50 2	80 4	12	8	101 2	103 6	12	12	3 14
22	130	115	136	192	49 5	69 8	12	16	99 6	104 6	13	30	3 25
23	135	110	140	160	52 8	68 4	10	16	98 9	101 4	13	30	
24	120	105	96	150	33 4	50 0	6	6	100 6	101 0	13	Recovered	
25	125	130	120	116	49 4	51 2	10	8	100 1	98 9	13	Recovered	
26	125	105	66	172	42 2	43 3	8	10	103 2	102 4	13	Recovered	
27	130	120	160	192	43 7	60 3	10	16	102 4	102 4	18	Recovered	
28	130	120	132	180	50 0	66 4	10	12	100 6	99 3	18	Recovered	
29	120	120	112	160	46 3	53 6	6	12	101 2	102 4	18	30	
30	125	114	84	160	44 0	54 2	10	10	98 8	98 8	18	Recovered	
31	115	140	120	192	47 7	63 0	8	12	99 0	98 2	18	Recovered	
32	125	115	120	200	55 8	76 3	16	12	98 4	103 6	18	{ 25 hrs 25 min }	3 29
33	130	115	104	160	43 5	60 3	6	8	99 7	104 4	18	Recovered	
34	125	115	120	120	52 3	60 7	6	8	101 2	99 0	18	Recovered	
35	126	120	72	72	53 0	67 5	10	8	100 8	99 8	18	Recovered	
36	110	110	140	180	52 0	60 0	16	14	101 6	99 8	18	Recovered	
37	130	110	110	150	12		12	10	101 4	102 3	18	Recovered	
38	135	100	112	188	55 2	66 7	10	16	102 2	104 3	18	Recovered	
39	132	80	72	160	37 0	44 2	8	8	100 2	102 6	18	Recovered	
40	Average fall 16 88 Mm Hg		Average rise 53 00 per min		Average rise 28 5% over control values		Average rise 1 88 per min		Average rise 85° F		7	Average survival time 26 33 hrs (excluding survivals)	Aver- age 3 26%

* The animals listed as recovered were in most instances sacrificed three to four days following removal of the pneumatic cuff. Longer survival periods are being studied at the present time.

TABLE III
BLOOD AND URINARY FINDINGS FOLLOWING EXPERIMENTAL CRUSH INJURIES

Expt No	Plasma Creatinine* Mg %			N P N Mg %			Urinary Creatinine* Mg /Cc			Urinary Output Cc			Urine Benzidine Reaction		Urine Albumin	
	Con- trol	After Press Removed	Reading 4-6 Hrs	Con- trol	After Press Removed	Reading 4-6 Hrs	Con- trol	After Press Removed	Reading 4-6 Hrs	Total While Press on Thigh	Total for 4-6 Hrs After Press Removed	48	Con- trol	After Press Removed	Neg	Pos
1	1 9	2 0		1 5	1 4		0 5	5 7					1 4	1 5		
2	2 2	3 9		6	9		1 0	4 5		3 2	1 2	45	Neg	Pos	Neg	Pos
3	1 9	17 4		9	1 5		2 8	1 1		2 2	1 7	4	Neg	Pos	Trace	Pos
4	8	3 6		9	1 9		30 0	84 0	5	2 4	1 7	26	Neg	Pos	Neg	Pos
5	4	12 8		1 0	3 2		35 2	84 0	8	9	1 6	3	Neg	Pos	Trace	Pos
6	1 1	20 1		1 0	1 8		31 0	71 6	9	2 5	1 5	3	Neg	Pos	Neg	Pos
7	2 3	11 6		9	2 3		30 0	63 7	1 1	2 1	7	20	Neg	Pos	Neg	Pos
8	4	5 5		1 1	1 5		27 5	81 0	1 0	2 5	1 1	42	Neg	Pos	Neg	Pos
Average rise 8 2 mg %			Average rise 8 mg %			Average rise 43 2 mg %			Average rise 2 8 mg %			Average fall 7			Av 37 cc	
															Av 23 9 cc	

* No selection was made as to sex, age or regulation of carbohydrate and protein intake of the animals prior to the experiments. This probably accounts for the high plasma creatine and creatinuria of the control specimens. Control values on 12 animals under the same conditions showed similar results and human specimens showed normal values.

TABLE III—Continued
Microscopic Examination of Urine—
Catheterized

Exper No	Urine Reaction (Litmus)		Gross Appearance of Urine		Microscopic Examination of Urine— Catheterized		Blood Pressure		Pulse		Hematocrit		Therapy and Result
	Con- trol	Reading 4-6 Hrs After Press Removed	Control	Reading 4-6 Hrs After Press Removed	Control	Reading 4-6 Hrs After Press Removed	Con- trol	Reading 4-6 Hrs After Press Removed	Con- trol	Reading 4-6 Hrs After Press Removed	Con- trol	Reading 4-6 Hrs After Press Removed	
1	Acid	Alk	Clear yellow	Grossly bloody	Occasional leukocyte and epithelial cell No erythrocytes or casts	Loaded with erythro- cytes Numerous leu- kocytes and epithelial cells Numerous red cell casts and granular casts	130	120	132	180	50 0	66 4	Pneumatic cuff applied Recovered
2	Acid	Acid	Clear amber	Grossly bloody	Occasional leukocyte and epithelial cell No erythrocytes or casts	Loaded with erythro- cytes Few leukocytes and epithelial cells	130	115	160	102	43 7	60 3	Pneumatic cuff applied Recovered
3	Acid	Alk	Clear yellow	Dark brown	Occasional leukocyte No casts No erythro- cytes Occasional epithelial cell	30-40 erythrocytes Numerous epithelial cells Few leukocytes	130	85	112	200+	42 2	67 7	No therapy Died
4	Alk	Acid	Slightly cloudy yellow	Cloudy grossly bloody	2-3 epithelial cells Occasional leukocyte and erythrocyte	Loaded with erythro- cytes Numerous epithelial cells 6-8 leukocytes/H P F No casts	135	100	112	188	55 2	66 7	Pneumatic cuff applied Recovered
5	Acid	Alk	Clear yellow	Grossly bloody	Occasional leukocyte and epithelial cell No casts or erythrocytes	Loaded with erythro- cytes 3-4 granular and red cell casts/ H P F Numerous epithelial cells and crystals	120	45	172	200+	50 4	76 4	No therapy Died
6	Acid	Alk	Clear amber	Grossly bloody, brown tinge	Occasional erythro- cyte epithelial cell and leukocyte No casts	No casts Loaded with erythrocytes Numer- ous epithelial cells and crystals	130	60	104	180	53 2	78 0	No therapy Died
7	Acid	Acid	Clear yellow	Grossly bloody, brown tinge	Occasional granular cast Occasional epi- thelial cell and leuko- cyte Occasional erythrocyte	Loaded with erythro- cytes Numerous red cell casts and large brown granular casts	125	120	132	180	50 2	73 6	Pneumatic cuff applied Died
8	Acid	Alk	Clear yellow	Grossly bloody brown tinge	Occasional leukocyte and epithelial cell No casts or erythro- cytes	Loaded with erythro- cytes Numerous epithelial cells Occa- sional granular cast	120	115	152	180	40 8	55 3	Pneumatic cuff applied Recovered
							Average fall 32 5		Average fall 53/min		Average rise 41 1% over control values		

CRUSH PERIOD

During the crush period there was no significant change in blood pressure in any of the animals. A slight increase in the concentration of the red blood corpuscles was noted in 22 experiments and a slight decrease in 18, the average being an increase of 61 per cent. The pulse rate increased in 30 experiments, decreased in eight and remained unchanged in two, the average being a rise of 20.8 beats per minute. The respiratory rate increased in 23 experiments, decreased in 12 and remained unchanged in five. The average was an increase of 2.3 per minute. The temperature rose in 21 animals and fell in 16, the average being a rise of 36° F. There was an average fall in plasma creatinine of 69 mg %, and an average increase in plasma creatine of 48 mg % was observed. Nonprotein nitrogen values increased an average of 4.05 mg %. Urinary creatine decreased 0.7 mg per cc. Urinary creatinine decreased 30 mg per cc. Microscopic examination showed red blood cells in the urine in every case within two to three hours after the press was applied. The benzidine reaction became positive in two to three hours. Albumin was present in the urine in two to four hours. Except for the urinary findings, it is to be observed that the alterations in most of the functions were minimal.

RELEASE OF CRUSH WITHOUT THERAPY

There were 19 experiments in this group, the results of which are given in Table I. The press was applied to the thigh for a period of five hours. At the end of this time it was removed and the animal was observed, no form of therapy being employed. All animals died except one. Upon removal of the press there was usually a sudden sharp decline in blood pressure to 50 to 60 Mm Hg. The pressure returned within a few minutes to, or almost to, its former level and subsequently a progressive decline occurred. An increase in the concentration of the red blood cells occurred as soon as the press was removed. This increase was progressive and an average rise of 44 per cent over the control values was observed at the end of periods varying from two to six hours. The pulse rate rose an average of 72.7 per minute. The respirations increased an average of 12 per minute. The rectal temperature increased an average of 1.17° F. The average duration of life in this group was 7.55 hours.

The urine usually became grossly bloody within an hour after the press was removed. The output of urine in this group during the two- to six-hour period following removal of the press averaged 3.3 cc. Although granular and red blood cell casts were frequently found, the dark granular casts, which have been described in clinical cases of crush injury, were not observed.

In three dogs of this group, in which blood chemical and urinary chemical changes were observed, the plasma creatine increased an average of 15.6 mg % above the control levels. Plasma creatinine levels showed an average increase of 3.45 mg %, and nonprotein nitrogen an average rise of 44.8 mg %. Uri-

nary creatine increased an average of 1.03 mg per cc. Urinary creatinine decreased an average of .25 mg per cc.

RELEASE OF CRUSH WITH THERAPY

There were 21 experiments in which, following the removal of the press, a pneumatic rubber cuff was applied to the injured thigh at a pressure of 40 Mm Hg. When the cuff was applied for a period of 13 hours, three of six animals died. When the time of application was increased to 18 hours, three of 15 died. The average survival time of these six animals was 26.3 hours. The average fall in blood pressure of the entire group in the first four- to six-hour period was 16.9 Mm Hg. Hematocrit volumes increased in this same period an average of 28.5 per cent over the control values. The respiratory rate showed an average increase of 1.88 per minute, and the average elevation of body temperature was 85° F. The pulse rate increased an average of 53 per minute.

Just as in the untreated group, the urine became discolored and showed gross blood within one hour after the press was removed. The average urinary output for the same period of time was 36.2 cc. On microscopic examination of the urine, several animals showed granular and red blood cell casts and an occasional hyaline cast. Two animals of this group showed in the urine large dark brown granular casts which were similar in appearance to those described in clinical cases of crush injury. The urinary creatine output averaged 3.67 mg per cc. The creatinine output showed an average decrease of 1.27 mg per cc. Plasma creatine increased an average of 3.60 mg % and plasma creatinine an average of .57 mg %.

PATHOLOGIC CHANGES

The pathologic changes in the treated group of animals which ultimately succumbed were, as a rule, more marked than those of the untreated group, probably because the duration of life was longer, and there was a longer period of time in which anoxia could exert its ill effects. There was patchy, bluish discoloration of the lungs, which was most noticeable in the more dependent portions. Microscopically, there was engorgement of the alveolar vessels and extravasation of fluid and cells into the alveolar spaces. The liver showed dark discoloration and the cut surface was moist. On microscopic examination, engorgement of capillaries and degenerative changes in the hepatic cells were noted. The adrenals showed red discoloration on the cut surface, which was most pronounced in the medullary portion, and the vessels were engorged in both cortex and medulla. Degenerative changes were present in the cortical cells, and there was moderate infiltration of polymorphonuclear leukocytes in the zona fasciculata. The gastro-intestinal tract of several animals showed gross hemorrhage, this was greatest in the duodenum and the jejunum. The mucosa of the duodenum and the jejunum was hyperemic, and on microscopic examination, there was evidence of vascular engorgement. The peritoneal cavity of two animals and the pleural cavities

of one, contained free fluid. The kidneys were of normal size and on external examination showed no change. The cut surface was darkly discolored in both medulla and cortex. Red radial streaks, indicative of vascular engorgement, were present. Microscopic examination showed engorgement of the glomerular capillaries with extravasation of blood into Bowman's capsules. In some animals homogeneous, amorphous eosinophilic material was present in Bowman's capsules. Vascular engorgement was evident in both cortex and medulla. The collecting tubules in many areas were dilated but empty, and the lining epithelium was flattened. No large brown casts were found.

Examination of the injured extremity revealed massive swelling of the thigh, and to a lesser extent of the leg and foot. There was some swelling of the flank and of the adjacent anterior abdominal wall. Upon section, the swelling was seen to be due to the presence of clear yellow fluid in the subcutaneous tissues, the fascial planes, and the bellies of the muscles. In only two animals which succumbed was there extravasation of whole blood into the tissues of the limb, and in these the amount was very small. The swelling persisted for at least several days. Necrosis and sloughing of the skin were frequently noted at the site at which the maximum pressure had been applied. The pressure resulted in temporary paralysis of the extremity.

DISCUSSION

The type of injury which has resulted in the so-called crush or compression syndrome has, in all reported cases, involved the extremities, and has been of sufficient violence to crush large masses of tissue, especially skeletal muscle. The victims have remained pinned beneath the fallen object for several hours, resulting in great interference with the circulation of the entire extremity and in some instances in the production of necrosis at the site of injury. Following removal of the constricting object, with reestablishment of the blood supply, swelling of the extremity appears. Shortly afterward the patient may present signs of shock and later may develop renal failure. As stated previously, one of the objects of the present experiments was to attempt to reproduce the crush syndrome. When the press described above is applied to an extremity for a period of five hours at a pressure of 500 pounds, the tissues of the thigh are crushed and at least a major portion, if not all, of the blood supply to the part is interrupted for the duration of this period. The popliteal and posterior tibial pulses cannot be felt with the press in place, but are always palpable immediately after its removal. Following the removal of the press there is progressive swelling which seems to reach its maximum in six to eight hours. As can be seen from Table I, shock was produced in all experiments, and was fatal in all animals except one in the untreated group.

The swelling of the extremity is due almost entirely to extravasation of plasma rather than of whole blood. The fluid observed in the tissues of the extremity and the adjacent body wall was a clear yellow, very rarely was there even slight evidence of whole blood loss. At autopsy, the posterior part of the animal's body was bisected and the weights of the injured and uninjured

sides were compared. This comparison revealed a fluid loss in the injured side of 3.26 per cent of the body weight. The results of previous experiments⁹ of approximately the same duration in which plasma was removed from the blood stream indicate that the local loss in the present experiments was the major factor in causing the decline in blood pressure and death. Probable explanation for the plasma loss lies in the local mechanical injury to tissues plus the anoxia produced by the constricting or tourniquet effect of the press.

Further evidence of plasma loss is demonstrated by the marked increase in the concentration of the red blood corpuscles which invariably occurred. This rise began immediately after the press was removed and progressed in the untreated group until the animal died. The average rise in the untreated group was 44 per cent above the control values as compared with 28.5 per cent above the control values in the treated group.

In the animals which were successfully treated by application of the pneumatic cuff there was comparatively little swelling of the injured extremity at the time of removal of the cuff after 13 or 18 hours. Swelling became more evident within a few hours and appeared to become greater in those treated for 13 hours than in those to which the cuff was applied for 18 hours. In animals which died in spite of treatment, comparison of the weight of the injured and uninjured sides showed a fluid loss as great as that of the untreated group (3.26 per cent of body weight). The beneficial effect of the pneumatic cuff would appear to be due chiefly to its rôle in lessening local fluid loss into the extremity. It is likely that a partial repair of the increased capillary permeability in the injured extremity takes place following the return of its blood supply during the 18 hours that the pneumatic cuff is in position.

The urinary changes in these experiments are of interest. Blood was present, on microscopic examination of the urine, within two to three hours after the press was applied. The development of hematuria probably precedes an appreciable diminution in blood volume and blood pressure, and also probably precedes the absorption into the general circulation of the major part of the products of injury. There may be some absorption of these metabolic products at the upper end of the press and through collateral channels where the circulation is still intact. Gross blood was present in the urine within an hour after the press was removed. A peculiar brownish discoloration of the urine was often noted during the period following removal of the press. Oliguria was observed in all experiments, most severe in the untreated animals and in those which died in spite of treatment, that is to say, those animals in which shock was most profound. This oliguria was due at least in part to the physiologic imbalances accompanying shock—diminished blood volume and flow, depression of blood pressure, and hemoconcentration. Granular and red blood cell casts were frequently found and occasionally hyaline casts were noted, but in no animals of the untreated group, and in only two of the treated group, were large, brown granular casts observed. In these two animals, histologic examination did not show the selective tubular changes and the casts which have been described in clinical cases of crush injury. Had the

length of life been greater, it is possible that this observation would have been made more often

Elevated blood creatine levels and creatinuria have been observed in several types of muscular disease¹⁰ Aub and Wu¹¹ have reported an increase in blood creatine following injuries to muscle. The values we have obtained are high, and are suggestive of severe muscle damage. Marked disturbance of creatine-creatinine ratios in blood and urine were observed. The levels are higher in the plasma of the untreated group than in that of the treated group, and higher in the urine of the treated group than in that of the untreated group. These observations may indicate failure of excretion of the excessive creatine because of diminished renal function. Destruction of renal function in itself will produce an elevation in blood creatine^{12 13}. Further evidence of diminished renal function and tissue injury is presented by the progressive rise in nonprotein nitrogen seen in all the experiments.

The method which has been described presents both advantages and disadvantages in the study of shock. Included among the advantages is the observation that there appears to be less individual variation in the responses of animals to this form of injury than to any other that we have studied. This method allows one to study, with greater exactness, the pathogenesis of shock, and to determine, with greater certainty, the effects of various therapeutic procedures. Another advantage which is common to all methods in which one extremity is injured is that the opposite extremity can be used as a control. A disadvantage of the method is that the type of injury which is produced is not encountered as frequently in patients as are burns and some other types of trauma.

It remains to be proved whether or not the crush syndrome as observed in patients can be reproduced by this method. The alterations in the urinary tract in the experimental animals and in the patients are not identical. Most of the animals which survived following treatment with the pneumatic cuff were sacrificed after several days, hence a study of the late effects of injury is incomplete. Such studies are being carried on at the present time. It will probably be necessary to modify the method in such manner that the survival period of untreated animals will be lengthened. It is apparent that a careful study of renal function in this experimental condition is indicated.

SUMMARY

A new method for producing shock, in which an attempt is made to simulate the crush syndrome as observed in patients, is described. The method consists in placing a posterior extremity of the anesthetized animal in an apparatus with uneven surfaces, which exert great pressure on the soft tissues.* Removal of the extremity from the press is followed by swelling of the leg, an increase

* It is to be emphasized that medium sized animals which had a good deal of muscular tissue in the thigh were chosen and that the grooves in the insets of wood on the press allowed the pressure to be made mainly on the soft tissues rather than on the femur.

in the concentration of the blood, a decline in blood pressure, oliguria, abnormal urinary findings, elevated blood creatine and creatinuria, and usually death. The local loss of plasma is great. Recovery usually results if, at the time the press is removed, the injured part is placed immediately in a pneumatic tube with an internal pressure of 40 Mm Hg.

Whether the experimental conditions have any relationship to the crush syndrome as observed in patients remains to be proved, but it can be stated that the use of this method results in a more uniform production of traumatic shock than any with which we have hitherto worked.

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FURTHER OBSERVATIONS ON STAB WOUNDS OF THE HEART

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I SHOULD like to report upon three points concerning the subject of penetrating wounds of the heart. Noteworthy achievement in the repair of these wounds has been accomplished by Elkin,¹ of Atlanta, Bigger,² of Richmond, and Griswold,³ of Louisville. Contributions to the subject have been made also by numerous other surgeons. The writer has had little or no experience with patients who were brought to the operating room because of a stab wound of the heart. He has accidentally made wounds of the heart while carrying out other operations upon this organ in the human, and these wounds have had to be repaired. He has had considerable experience with the heart in the experimental laboratory. Whether the wound is in the human heart or in the heart of a dog, the methods of handling it are the same. Because of this, I feel that I can make a few additions to the subject.

The best way to stop bleeding from a ventricle is by placing a finger *upon* and not *in* the wound. It is difficult, or impossible, to keep the finger on the wound because of the movement. It slides off and there is a squirt of blood. However, it can be kept on the wound fairly well, if the heart is steadied by a suture. This can be done by placing a suture in the apex of the heart and holding this suture between the thumb and third finger of the left hand while the index finger of that hand is placed upon the wound. In this way the hand moves with the heart and you do not get so many squirts of blood. The apex was selected for this suture because this region is farthest from the major coronary arteries, and there is least likelihood of inflicting injury to one of these important arteries in this location. Often the surgeon wants to place this suture without delay because of bleeding. To inspect the heart in order to find a place for the suture takes time. The apex is always a favorable place for it. These points originated, I believe, from experiments upon dogs.⁴ Griswold describes this "hot-spot" in the operation as follows: "There is nothing more disconcerting than to hold in one's hand a writhing, jumping heart and blindly attempt to find a wound deep in a gushing whirlpool of blood. The insertion of a traction suture converts this stage of the operation from futile blundering into an orderly process. The traction suture steadies the jumping organ so that a finger may be placed over the opening to temporarily staunch the flow."

The next step consists of closure of the wound. According to the original method, a traction-suture was placed on each side of the finger, crossed, and held under gentle traction by the assistant. The finger was then taken off the wound. These traction-sutures were supposed to stop the bleeding, and the wound was then closed by permanent sutures. Elkin modified the method by placing a temporary suture under the finger and across the wound. Traction on this suture stopped the bleeding. Bigger and Griswold have used

Elkin's modification of this technic to good advantage, and it seems to be the method of choice. If the wound lies along a coronary artery, the method should be such that the artery is spared. The original method spared this artery. The traction-suture on each side of the finger was placed under vision so that these sutures would not get the artery. The wound was sutured under vision so that the artery could be spared in these sutures. Interrupted sutures were used in the illustration of the method. A mattress suture was not illustrated. An illustration of a mattress suture for closure of a wound close to an artery is shown in Figure 1. Griswold also recommends a mattress suture for wounds adjacent to an artery.



FIG. 1.—Method for repair of wound situated adjacent to coronary artery. The wound can be closed by one or more mattress sutures without sacrificing the coronary artery.

The type of wound to which I refer is illustrated in Figure 2, taken from a paper by Olim and Hughes.⁵ A quotation from this article follows: "There was a laceration 1.5 cm. in length on the anterior surface of the left ventricle, approximately 2 mm. to the left of the left anterior descending coronary vessels and about 5 cm. from the apex (Fig. 2). The laceration penetrated the chamber of the left ventricle, and as soon as the tamponade was released, great streams of blood spurted. A silk traction-suture was placed in the apex, as described by Beck, in order to steady the heart. An attempt was made to close the laceration with silk sutures and to avoid the coronary vessels, but due to the narrow band of myocardium between the laceration and the vessels, this was found to be impossible, as the sutures pulled through the frayed muscle on two attempts. Because of the critical condition of the patient and the excessive blood loss taking place, it was thought unwise to

make further efforts at preserving the coronary vessels Four interrupted silk sutures were then placed so that the vessels were encircled and the laceration closed " Electrocardiographic evidence of a myocardial infarct developed The patient recovered

Davenport, Blumenthal, and Cantil⁶ reported a patient who had a stab wound of the heart "The puncture which caused the bleeding into the pericardial sac was found at the apex of the left ventricle and corresponded in size to the point of an ice-pick It was situated one millimeter from the coronary artery and vein The wound in the heart wall was not spurting

blood, but it was considered advisable to suture the wound to prevent subsequent hemorrhage Three sutures of black silk were placed in the heart with a curved needle The first suture was left long as a guide The other two were placed around the wound including the left descending coronary artery and vein, one above and one below " Electrocardiographic evidence of infarction in the anterior wall of the heart was obtained after operation The patient recovered

Badertscher⁷ reported a patient who was stabbed in the heart "On incising the pericardium from base to apex, the

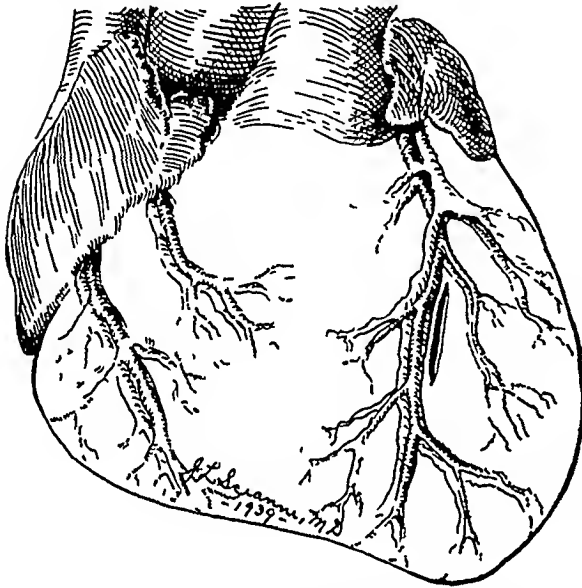


FIG 2—Wound of left ventricle situated adjacent to descending ramus of left coronary artery Coronary artery and vein were sacrificed by the sutures (Olin and Hughes, Jour Thoracic Surg, 9, 99, 1939)

hemorrhagic tamponade was released and the heart resumed rapid activity, resulting in a terrific hemorrhage The laceration in the heart was 6 Mm long, and had perforated the right ventricle immediately adjacent to, and parallel to, the right border of the descending ramus of the left coronary artery in its proximal third Hemorrhage was controlled by silk sutures deep in the ventricular wall, parallel to the laceration on either side Free ends of the sutures were twisted to form a single strand on each side of the wound and then tied over the wound as a single suture Several such sutures were required to control the hemorrhage Although the coronary artery was not encircled by the sutures, it must have been occluded by the inverting effect On control of hemorrhage from the heart, the blood pressure immediately rose to 120/80 and became stable The heart, observed for 15 minutes, became progressively cyanotic, most markedly at the apex The chest wall was closed in layers As the skin sutures were being applied, the blood pressure suddenly disappeared This was approximately 25 minutes after occlusion of the coronary artery In retrospect, we feel that it is possible that this patient's life might have been saved had deep sutures been used to close the heart wound, thus leaving the coronary vessels unobstructed on the surface of the

heart Some of these important technicalities, unfortunately, are overlooked when one is working under pressure, and on such an elusive object as a rapidly beating heart "

I can appreciate Badertscher's feeling in this regard I recall, as though it were yesterday, an experience that I had in 1931 I tore a hole in the right auricle in the region where the superior vena cava joins the auricle I was dissecting a tuberculous scar from the auricle when this occurred I

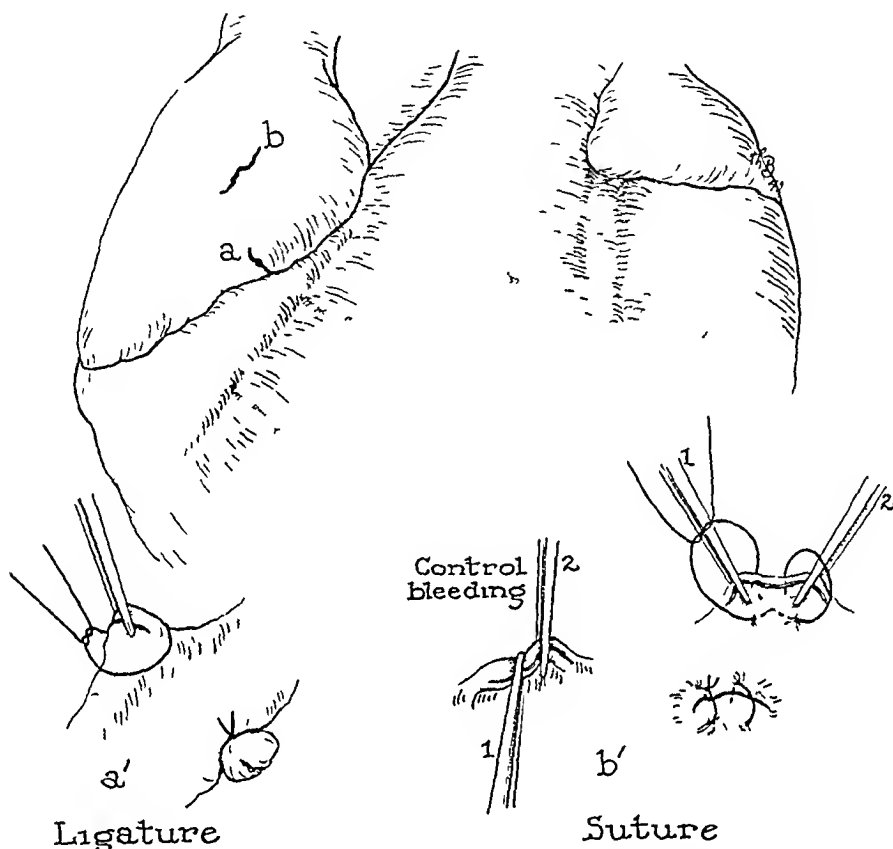


FIG 3—Methods for the repair of auricular wounds Auricular wall can be taken in a hemostat without crushing it A wound along the margin of the auricle can be repaired by a ligature as in (a) A wound elsewhere, as in (b), is repaired by picking up the edges of the wound in hemostats and bringing the points close together to stop bleeding Sutures are then placed for closure

followed my first impulse and placed a finger upon the tear It was utterly ineffective Blood poured out from beneath my finger and I could not see the wound After losing about 500 cc of blood, or more, the wound was exposed and the margins of the wound were taken in clamps and easily sutured It was not a difficult tear to suture after it was taken in hemostats but the situation of placing a finger upon the wound was very bad indeed In our laboratory we often tear an auricle in dissection of coronary arteries As a rule, it is an easy problem to handle The margin of the wound is picked up in a small hemostat and the wound is either closed by suture or by mass-ligature The ligature is good if the wound is at the margin of the auricle (Fig 3) The use of clamps for the repair of auricular wounds was described by me in 1934,⁸ and by Elkin,¹ in 1941

I have often stopped bleeding from the surface of the heart by placing a superficial suture in the muscle at the bleeding point and tying a small muscle graft into the suture A small muscle graft can stop bleeding from a coronary

vein. It can be loosely anchored over coronary vein and coronary artery in such a way that the vein does not bleed and the artery is not occluded.⁹ Bigger¹⁰ sutured the pericardium into a wound for closure. In his case the

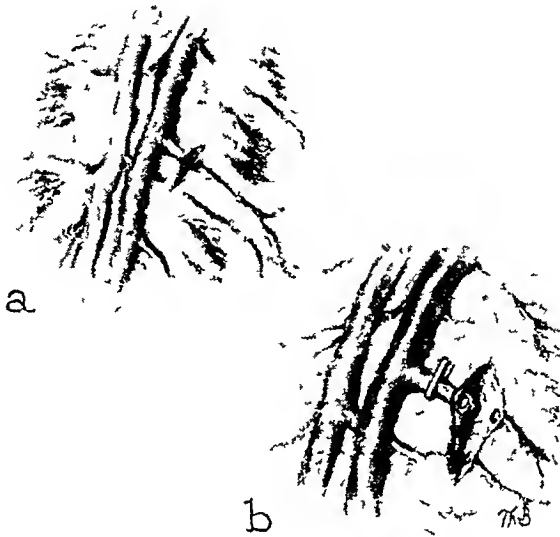


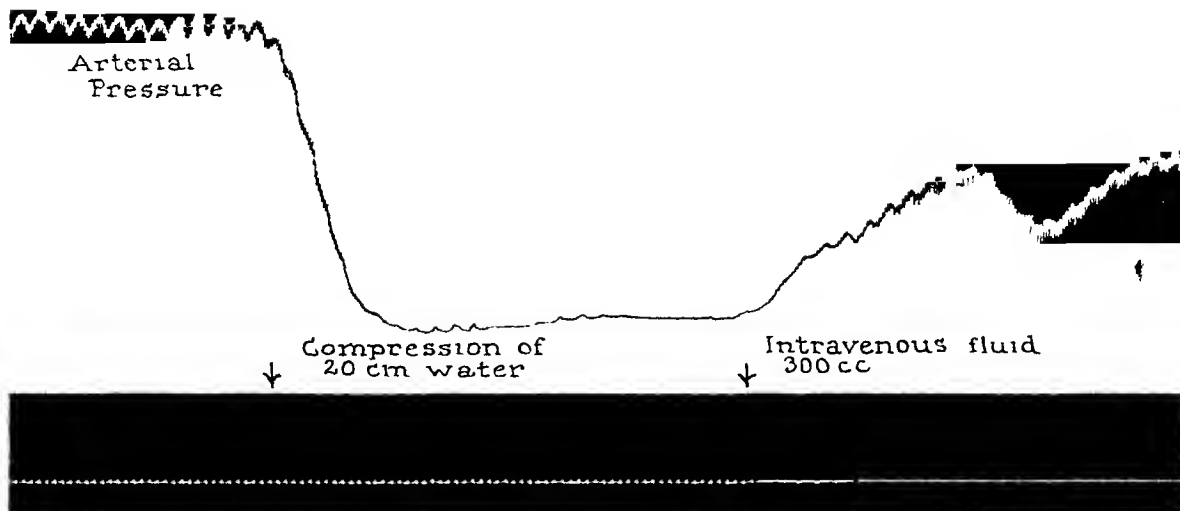
FIG 4—(a) Branch of major coronary artery severed close to its origin
(b) Magnification of same. This artery occluded by brain clip without injury to main artery.

muscle was very soft and friable and sutures had a tendency to tear out. Cushing's brain clip is sometimes useful (Fig 4). Perhaps Bigger¹¹ might have found a clip useful in one of his cases. In his case "the injury was so close to the main stem of the artery that it was felt that if an attempt was made to ligate the injured vessel which had stopped bleeding, it would in all probability be necessary to ligate the main artery. It was decided, therefore, that it would be better to close the operative incision and take the chance of having to re-open it if bleeding and tamponade occurred." The patient recovered.

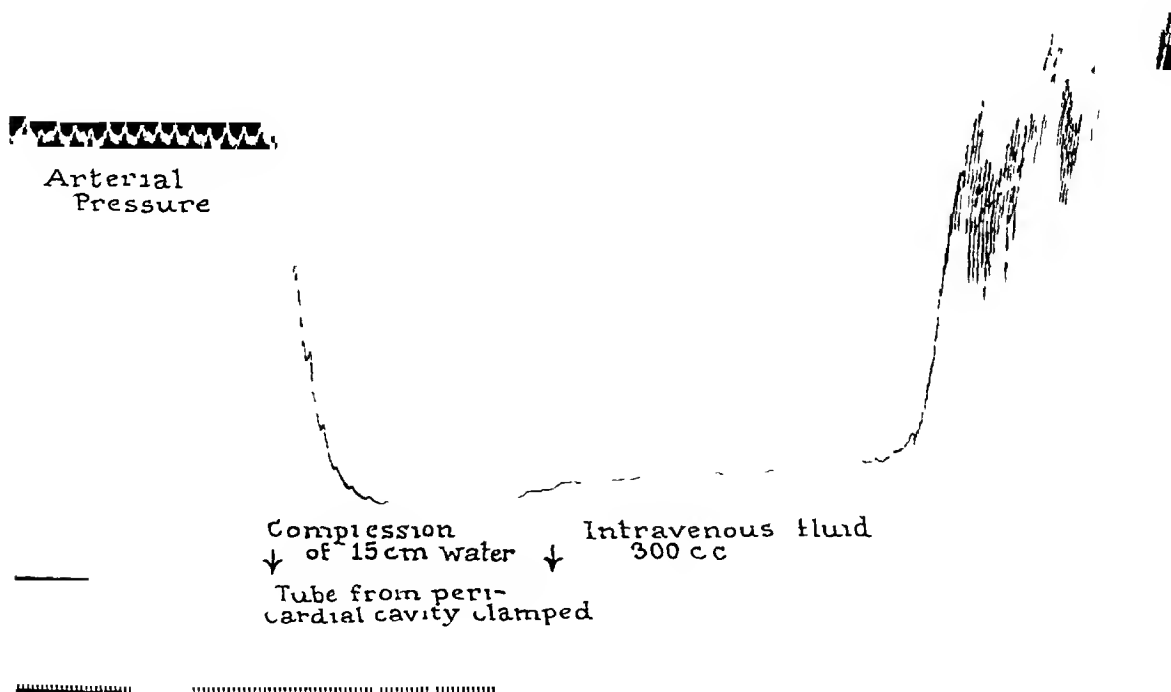
In 1933, Bigger and Wilkinson¹² described a method which they employed satisfactorily for the repair of a stab wound of the superior vena cava. A finger was placed under the vena cava and the vein was elevated. This collapsed the vein and stopped the bleeding. The wound was successfully sutured.

The other point that I should like to discuss concerns the administration of fluid intravenously in patients with acute compression of the heart. Bigger advocates the administration of blood, acacia solution, glucose or sodium chloride solution as a preoperative measure in patients who have received a stab wound of the heart. Griswold states that intravenous fluids, particularly blood, should be administered when hemorrhage has occurred but are of little value preoperatively in case of tamponade.

Two types of experiment are interesting in this connection. In one type (Graph 1) the heart is compressed by a force of 20 cm of water. The arterial pressure falls and remains low. This compression force is kept on the heart at 20 cm and 300 cc of fluid is given intravenously. The arterial



GRAPH 1—Experiment Arterial pressure was recorded. Cannula attached to parietal pericardium and 20 cm of pressure applied to heart. Fluid was given intravenously while the pressure was maintained at 20 cm. Some fluid was allowed to escape from the pericardial cavity in order to keep the pressure on the heart at this level. The administration of fluid intravenously produces a rise in arterial pressure under these conditions.



GRAPH 2—Experiment Arterial pressure was recorded. Cannula attached to parietal pericardium and 15 cm of pressure applied to heart. After this pressure was established, a clamp was placed upon the tube so that none of the fluid could escape from the pericardial cavity. Fluid was then given intravenously. The arterial pressure did not rise.

pressure rises when the fluid is given. In the other type of experiment (Graph 2) the heart is compressed by a force of 15 cm of water. A clamp is placed on the tube leading to the pericardial cavity so that fluid cannot escape from the pericardial cavity. The quantity of fluid in the pericardial cavity is fixed. The arterial pressure falls and remains low. Fluid, 300 cc, is given intravenously. The arterial pressure does not rise.

It appears, then, on the basis of such experiments, that the administration of fluid intravenously produces a rise in arterial pressure if the degree of compression on the heart is fixed and does not rise to higher levels, as the venous pressure rises when fluid is given intravenously. For this to occur some of the fluid must escape from the pericardial cavity. If the quantity of fluid in the pericardial cavity is fixed and none of it can escape then the administration of fluid intravenously does not result in a rise in arterial pressure. As the venous pressure goes up, the degree of compression also goes up.

The one experiment applies to the patient with compression in whom some blood is escaping from the pericardial cavity. The administration of fluid intravenously has a beneficial effect in this patient. The other experiment applies to the patient with compression in whom there is no blood escaping from the pericardial cavity. The wound in the pericardium has become sealed. The administration of fluid intravenously does not produce a rise in arterial pressure in this patient.

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DIAPHRAGMATIC HERNIA OF CHILDREN⁺

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DIAPHRAGMATIC HERNIA occurring in infants and children presents many problems of diagnosis and treatment that differ markedly from those caused by such herniae occurring among adults. One of the principal reasons for this variation is the difference in the types of diaphragmatic hernia which are most commonly encountered in these periods of life.

Although any of the various types of diaphragmatic hernia may be encountered in any period of life, the more common types seen among infants and children, in order of frequency, are those due to embryologic structural defects of the diaphragm, namely, pleuroperitoneal hiatus herniae and those caused by congenital absence of the diaphragm. Next in probable order of frequency are esophageal hiatus and traumatic herniae.

TABLE I

DIAPHRAGMATIC HERNIA

SITE OF OPENING AND CONTENTS OF HERNIA IN 304 ADULTS AND CHILDREN

Site of Opening	Adults	Children	Contents of Hernia	No of Cases
Esophageal hiatus	222	5	Stomach (omentum)	215
			Stomach omentum and spleen	4
			Stomach and colon	8
Esophageal hiatus with short esophagus	15	0	Stomach only	15
Hiatus pleuroperitonealis	2	6	Right colon and small bowel	4
			Colon, small bowel stomach and spleen	4
Absent posterior fourth of left diaphragm	1	6	Stomach colon small bowel and spleen	4
			Colon and small bowel	2
			Colon appendix small bowel and spleen	1
Foramen of Morgagni (subcostosternal)	5	0	Omentum only (2) and fat (1)	3
			Colon and omentum	1
			Omentum cecum, appendix, colon and terminal ileum	1
Left hemidiaphragm	37	4	Stomach only	5
			Stomach and colon	10
			Stomach colon, small bowel (24) spleen (15) and liver (8)	26
Right hemidiaphragm	1	0	Stomach duodenum colon small bowel liver (gallbladder) and head of pancreas	1
Total	283	21		304

In adult life the most common type of diaphragmatic hernia encountered is that which occurs through the esophageal hiatus. Although this type of hernia may be considered congenital in origin, the actual herniation often does

* Read before the Southern Surgical Association, Pinehurst, N C, December 9, 1941

not occur until late in life. Other types of diaphragmatic hernia occurring among adults, listed in the probable order of frequency, are traumatic herniae, subcostosternal (foramen of Morgagni) herniae, and those resulting from structural deficiencies of the pleuroperitoneal membrane.

In a series of 304 cases of diaphragmatic hernia in which operation was performed at the Mayo Clinic, 283 of the patients were adults and 21 were children 12 years of age or less. The relative frequency of the occurrence of the various types of hernia among adults and children and the abdominal viscera involved in the hernia in this series are shown in Table I.

The reason for the relative infrequency of those herniae that occur through structural defects of the diaphragm among adults is that most of the infants who are born with this type of hernia die in the first few hours or days of life of cardiac or respiratory difficulty resulting from the marked unilateral alteration in intrathoracic pressure at a time when the compensatory respiratory and cardiac reserve has not been developed to a sufficient degree to maintain function. However, if the respiratory and cardiac mechanisms are able to compensate for the presence of the abdominal viscera in the thorax, the patients may reach childhood or even adult life without any great amount of disability or symptoms, provided that intestinal or gastric obstruction does not develop. When the stomach is involved in these herniae, it usually becomes markedly dilated and the patients often have symptoms of partial gastric obstruction. Intestinal obstruction may occur owing to bands of adhesions between the omentum and loops of bowel, owing to inflammatory conditions of the bowel, or owing to appendicitis.

The clinical recognition of diaphragmatic hernia on the basis of subjective symptoms alone is often difficult. The symptoms are complex because of the various structures involved in the hernia. They depend on the amount of mechanical interference with the function of the herniated abdominal viscera, on the degree of the impairment of the normal function of the diaphragm, and on the amount of increased pressure within the thorax causing impairment of respiration and circulation.

The urgency of establishing a diagnosis is not as great in the case of adults as it is in the case of infants. In the latter case it is extremely important to establish a diagnosis as soon as possible. Many of these infants are born with a rapid, feeble pulse, are cyanotic, and are often considered to have cardiac disease. When infants present symptoms of cardiac or respiratory difficulty the thorax should be examined immediately, if possible, a roentgenogram should be made, and if a hernia is present, treatment should be instituted immediately.

The pleuroperitoneal hiatus types of hernia and herniae due to congenital absence of the diaphragm, which are the most common types of diaphragmatic herniae seen among infants and children, may be considered under one general heading as both of these types of hernia are caused by deficiencies of the development of the pleuroperitoneal membrane, which forms the posterolateral portion of the adult diaphragm.

The former (the pleuroperitoneal hiatus hernia) is due to a lack of fusion of the pleuroperitoneal membrane with the septum transversum, which results in a congenital continuity between the peritoneal and thoracic cavities. The opening is in the posterolateral portion of the diaphragm but varies with the amount of deficiency which has occurred in the formation of the pleuroperitoneal membrane. The opening is usually triangular or elliptic in shape and may be entirely within the diaphragmatic muscle posterolaterally, or there may be no diaphragm posteriorly with a triangular shaped opening reaching to the thoracic wall laterally with its apex toward the central tendon. In this type of hernia the abdominal viscera which usually are involved are the cecum (appendix), ascending colon, greater portion of the transverse colon and practically all of the small intestine. In the larger herniae which present posteriorly, the spleen may be involved. The stomach is usually in the abdomen. It may be markedly dilated and at times extend into the pelvis.

In the second type of congenital hernia, which is due to absence of the posterior portion of the diaphragm, there is a much larger deficiency caused by lack of formation of that portion of the diaphragm derived from the pleuroperitoneal membrane and probably the wolffian body. There are various gradations of the amount of the defect so that the size of the opening varies with the amount of the deficiency of the formation of the diaphragm. It usually amounts to approximately a fourth of the hemidiaphragm posteriorly, from the angle of the ribs laterally to the median portion of the diaphragm close to but not involving the esophageal hiatus. In this type of hernia the same abdominal viscera are involved as in the pleuroperitoneal hiatus types of hernia. The viscera involved are the ascending and transverse colon, small intestine and spleen, and, in addition, usually the stomach and occasionally the left lobe of the liver. The left kidney is usually elevated to a position above the level of the diaphragm in this type of hernia, while in the pleuroperitoneal hiatus type of hernia it is below the level of the diaphragm.

It is difficult to differentiate these two types of hernia clinically because the roentgenologic examination is often misleading in cases in which hernia results from congenital absence of the posterior portion of the diaphragm, as in many instances, at the time of the roentgenologic examination, the stomach is found to be in the abdomen and, at the time of the operation, it is found to be herniated into the left thoracic cavity. This I believe is due to the weight of the barium which causes the stomach to drop into the abdomen where it undoubtedly is a great deal of the time during life. It doubtless goes back and forth through the large opening posteriorly because the opening extends up to the esophageal hiatus. Because of the roentgenologic finding of the stomach in the abdomen, this type of hernia may be thought to be a true pleuroperitoneal hiatus type of hernia rather than due to a congenital absence of a larger portion of the diaphragm.

These herniae rarely have a hernial sac, and the abdominal viscera are in direct contact with the thoracic viscera. There is usually a failure of rotation of the colon and occasionally the small bowel is enveloped in a congenital

peritoneal fold which constitutes an internal hernia. In many instances there is a congenital malformation of the mesentery of both large and small intestines. This is very important surgically and great care must be exercised in replacing the intestines into the abdomen because of the danger of twisting the mesentery upon itself and obstructing the blood supply to the intestine. The herniated viscera produce marked or complete collapse of the left lung and often cause a marked shift of the mediastinum to the right. This shifting of the mediastinum depends on the amount of distention of the herniated abdominal viscera.

As I have stated previously, although the esophageal hiatus type of hernia may be considered to be essentially of congenital origin owing to defective formation of the esophageal hiatus, it usually does not occur until later in life. This type of hernia, however, may be of congenital origin and occur at birth, but the congenital occurrence of this type of hernia is relatively infrequent as compared to those herniae resulting from structural deficiencies of the diaphragm.

There are several types of esophageal hiatus herniae caused by the situation of the muscular defect of the hiatus. The most common site of the defect in the case of children is posterior. This type of hernia may be thought to occur through the aortic opening, but there is usually a small membranous portion of the defective hiatus in front of the aorta and the hernia does not occur through the anatomic aortic opening, which, in reality, is situated back of the diaphragm. The muscular defect of the hiatus in adult life is more commonly situated to the left of the esophagus and permits the stomach to extend into the posterior mediastinum and left side of the thoracic cavity. Occasionally, the muscular defect in the hiatus is situated posteriorly. In this instance, the herniated viscera extend into the right side of the thoracic cavity.

I believe that the occurrence of these esophageal hiatus herniae, both the congenital and acquired types, has a definite relationship to the embryologic formation of the posteromedian portion of the diaphragm as well as to the embryologic relationship of the descent of the stomach and the transverse septum. The transverse septum with the pleuroperitoneal membrane begins to migrate caudally in the 7-Mm embryo and rapidly passes the pulmonary buds and the anlage of the stomach, placing the greater portion of the lung in the pleural cavity and the anlage of the stomach partially above the diaphragm.

In the 11-Mm embryo, the stomach, which has been practically stationary, follows rapidly behind the descending septum transversum, and in the 17-Mm embryo it has virtually reached its permanent position. This descent is made possible by the sudden elongation of the esophagus. During this descent the right and left disopleural recesses are converted into bursae which surround the cardia. The left bursa usually disappears, and the right bursa, when well developed, is known as the "infracardiac bursa" and bears a definite relationship to congenital esophageal hernia.

Inasmuch as the stomach descends behind the septum transversum, if

there is a delay in descent of the stomach, the lumbar portion of the diaphragm will be imperfectly developed and the esophageal hiatus will be formed around the cardiac end of the stomach instead of around the esophagus. This will result in an abnormally large hiatus with deficiency both in the muscle ring and in the attachments of the diaphragmatico-esophageal membrane. The degree of the deficiency depends on the amount of gastric anlage in the thorax at the time of muscularization of the lumbar portion of the diaphragm. In rare instances, the stomach may remain in the elevated position as a result of a congenitally short esophagus and a partial thoracic stomach will result. In most instances, the esophagus continues to elongate normally, thus placing the stomach below the diaphragm. This abnormal position of the stomach will cause an abnormal enlargement of the esophageal hiatus with a wide space between the margin of the muscle and the wall of the esophagus. It will also result in imperfect fixation of the diaphragmatico-esophageal elastic tissue membrane to the esophagus and stomach and in an abnormally large peritoneal fold extending well down on the cardia of the stomach. This abnormal relationship will permit much more flexibility of the esophagus in the enlarged hiatus than is normal. The more defective the formation of the hiatus, the more likely is herniation of the stomach to occur through it in later life. The true congenital hernia, present at birth, may be explained in the same way, but it is probable that persistence of the dorsopleural recess may be a factor in the origin of congenital esophageal hiatus hernias.

In the series of 304 cases which I have operated upon, the relative incidence of traumatic hernia was slightly higher among children (19 per cent) than it was among adults (13.4 per cent). Traumatic diaphragmatic hernia may be caused by direct or indirect injury, or by inflammatory necrosis of the diaphragm. In cases of indirect injury of the diaphragm, the hernia may occur at any point, including points of embryologic fusion, but the most common sites are the dome and posterior half of the left part of the diaphragm. However, the injury may occur in the right part of the diaphragm. The laceration most commonly occurs in the posterior third of the left hemidiaphragm, it may be entirely within the suspended portion of the diaphragm, extending to but rarely involving the esophageal hiatus. It may extend to the thoracic wall and the diaphragm may be partially torn from its attachment to the thoracic wall. In case of direct injury of the diaphragm, the hernia may occur at any point and is usually the result of penetrating wounds, such as gunshot and stab wounds.

These traumatic herniae do not have a hernial sac, and the abdominal viscera are in direct contact with the thoracic viscera. The condition in these cases may be more properly termed "evisceration of the abdominal organs into the pleural cavity" rather than a "true hernia." The most common abdominal viscera involved in the hernia are the stomach, colon, small intestine, spleen, and occasionally the liver.

The most marked immediate symptoms usually are respiratory and circulatory embarrassment. The sudden onset of symptoms in cases of traumatic

hernia usually is directly attributable to the injury and there is rarely a question as to the clinical diagnosis. Surgical treatment is demanded because of the danger of cardiac and respiratory failure or because of intestinal strangulation.

SURGICAL TREATMENT

The urgency of and the indications for surgical treatment in the case of infants and children differ from those in the case of adults because of the more frequent occurrence of herniae caused by structural deficiencies of the diaphragm among infants and children. This type of hernia demands immediate surgical intervention because the longer the interval between birth and operation the greater the technical difficulties and the greater may be the hazard of operation. If operation is delayed for a long period, the abdominal viscera will have lost their right of residence in the abdomen, in that the abdominal cavity will not have developed sufficiently to contain them and there will be marked increase in the intra-abdominal pressure when the viscera are placed in the abdomen. At birth, the defect is relatively smaller in proportion to the size of the thorax than it is later in life. In the case of infants who live, the thoracic wall grows away from the posterior margin of the defective diaphragm because there is no posterior attachment. The opening which must be closed, therefore, becomes much larger as the child becomes older. Even though the diaphragmatic muscle is relaxed by interruption of the phrenic nerve, there may not be sufficient diaphragm to span this opening. In cases in which the hernia is due to congenital absence of the posterior portion of the diaphragm, the defect is often proximal to the left kidney and the pararenal fascia can often be utilized in completing and securing the closure after interruption of the phrenic nerve.

One of the chief dangers associated with the repair of these herniae is marked alteration of intrathoracic or intra-abdominal pressure. It is very important in these cases that the respiratory function be maintained by positive pressure during the operation and that at the completion of the operation a negative pressure be obtained and secured in the thoracic cavity. A roentgenogram should be made at the completion of the operation to insure that there is no shifting of the mediastinum owing to the pneumothorax. I do not permit the patient to leave the operating table until I have seen the roentgenogram. If there is any shifting of the mediastinum, more air is withdrawn to maintain the mediastinum in the midline.

I believe it is advisable to effect a temporary interruption of the phrenic nerve preliminary to repair of these herniae, as in some instances it may not be necessary for the resultant paralysis to be permanent. A piece of black silk is looped around the nerve and anchored to the posterior border of the sternomastoid muscle for future localization of the nerve if it is thought necessary to make the paralysis permanent. I do not think it is ever advisable to paralyze the diaphragm of an infant permanently unless it is essential to repair of the hernia, as such paralysis may lead to an eventration of the

diaphragm which may be associated with gastric and intestinal symptoms later in life. A temporary interruption of the phrenic nerve will paralyze the diaphragm for three to six months and, in the case of infants, I prefer to do this immediately preceding the abdominal repair of the hernia which is done under general anesthesia.

I prefer ether as the anesthetic agent for infants and cyclopropane for adults. In all herniae in which there is a direct continuity between the abdominal and pleural cavities I prefer intratracheal administration of the anesthetic agent by means of a positive pressure machine.

In the treatment of all herniae that have occurred through the left portion of the diaphragm, I prefer the abdominal approach by means of an oblique left rectus incision, starting at the ensiform cartilage and extending to the outer border of the rectus muscle. I believe there is less risk of the occurrence of thoracic complications when this approach is used. It is of particular advantage in cases of esophageal hernia as the herniated stomach is usually confined in a sac in the posterior part of the mediastinum and does not enter the true pleural cavity. Inasmuch as these abdominal viscera have herniated into the thorax, their true relationship can be more readily determined by following their course from the abdominal side, and if an injury to the stomach or other abdominal viscera occurs during the operation, it can be readily recognized and immediately repaired.

In the repair of herniae through the right portion of the diaphragm, I prefer the thoracic approach, because the large, right lobe of the liver makes the abnormal opening in the diaphragm inaccessible from the abdominal approach.

The technical difficulties of adequate exposure of the hernial openings through the left portion of the diaphragm and the esophageal hiatus are often considerable because of fixation of the left lobe of the liver to the leaf of the diaphragm. The exposure of these hernial openings is greatly facilitated by cutting the suspensory ligament and retracting the left lobe of the liver to the right. This can be accomplished, when the left lobe is small, by folding it on itself, and when it is large, by retracting it forward into the wound. The spleen is often very adherent to the posterior part of the diaphragm and hernial openings, but usually can be separated from these structures by blunt dissection. In some instances the spleen has been so injured and so firmly fixed in its abnormal position by adhesions that it cannot be separated from the hernial opening without serious injury. This not uncommonly occurs in the traumatic types of hernia and occasionally in esophageal hiatus herniae. In such instances, splenectomy is necessary.

In congenital herniae of infants, it is very important to remove carefully the herniated viscera from the thorax directly into the abdominal cavity and not permit the intestine to be exposed or injured with sponges any more than is absolutely necessary, as this adds a great deal to the shock of the operation. Great care should be exercised in carefully replacing the viscera in the abdomen so as not to produce a volvulus or interference with the blood supply.

After carefully replacing the viscera into the abdomen, the abnormal opening in the diaphragm is closed with interrupted silk sutures. In the case of adults, the tissues are first stabilized by interrupted silk sutures and then fascia lata which has been removed from the thigh, is interwoven between the overlapped layers and along the margin of the closure. The latter method is particularly advantageous in cases of traumatic herniae in which the diaphragm has been torn from the thoracic wall.

In all cases in which there has been a direct communication between the abdominal and the thoracic cavities, every effort should be made to reestablish the negative pressure within the pleural cavity by removing the air and by expanding the lung before the opening in the diaphragm is closed completely. In some instances, this cannot be accomplished until after the rent in the diaphragm has been closed. In some cases pneumothorax may push the mediastinum and heart to the opposite side and cause marked embarrassment of respiration and circulation. In these cases it is imperative that the mediastinum be stabilized in the midline immediately, by aspirating the air from the pleural cavity with a needle until the pressure becomes negative. I think it advisable to make a roentgenogram before the patient leaves the operating table, for the purpose of determining the amount of pulmonary expansion present.

Most patients are given a blood transfusion either during or immediately after the operation. The blood of every patient is grouped for transfusion before the operation. If the systolic blood pressure decreases to 90 Mm Hg, or less, the patient should receive a transfusion of blood. I believe it is very important to maintain blood pressure at a fairly constant level and not permit it to drop more than 20 Mm Hg below the normal preoperative reading. I prefer the use of blood transfusions to the intravenous use of solutions to maintain the blood pressure. Blood transfusions are also advisable in all cases in which the hernia is associated with loss of blood that produces secondary anemia.

If there is excessive mucus in the bronchi and lungs at the time of operation, it is imperative that it be removed by aspiration through the intratracheal tube used for the administration of the anesthetic agent, or by the use of the bronchoscope before the patient leaves the operating table.

On removing the patient to his bed, which has been made warm by hot water bottles, external heat is applied to the patient by use of additional hot water bottles. Fifty-eight to 60 per cent oxygen is administered in an oxygen tent until the patient has fully recovered consciousness, and the administration is continued thereafter as indicated. After the patient has fully regained consciousness, the oxygen may be administered with a nasal mask.

RESULTS

The results of operation in this series of 304 cases of various types of diaphragmatic hernia, in which 283 of the patients were adults and 21 were children, were as follows. There were 15 deaths following operation in the

entire series, on an operative mortality of 4.9 per cent. Eleven deaths occurred among adults and four among children. Of the 11 deaths among adults, nine occurred after operation for esophageal hiatus type of hernia, one after operation for repair of hernia due to congenital absence of the posterior portion of the diaphragm, and the remaining one after operation for traumatic diaphragmatic hernia. The cause of death in these 11 cases was pneumonia and pulmonary edema in five, cardiac disease and coronary sclerosis in three, cerebral embolism in one, pulmonary embolism in one, and mesenteric thrombosis in one.

Of the 21 infants and children operated upon, four died. Three died after operation for pleuroperitoneal hiatus type of hernia, and one after operation for repair of congenital absence of the posterior portion of the diaphragm. These children were 7, 9, 18, and 24 months of age, respectively, and in all instances death occurred within 48 hours after operation. One child died at the time of operation soon after the opening in the diaphragm had been exposed but before the repair of the opening had been begun. The causes of death of the four children were respiratory and cardiac failure, with partial atelectasis of the lung.

There were nine recurrences, all of which occurred among adults who had esophageal hiatus types of hernia. Of these nine patients, five had no recurrence of symptoms and recurrences were diagnosed because of a small protrusion of the cardia of the stomach above the diaphragm. Three of these five patients had a moderate shortening of the esophagus before operation. In this type of hernia it is not uncommon to find a small portion of the cardia above the diaphragm following operation. This may not progress and reoperation is not indicated unless there is recurrence of symptoms. In the case of the remaining four patients there was a definite recurrence of the hernia and subjective symptoms. A second operation was necessary for complete relief of symptoms in three cases and partial relief in the remaining case. There were no recurrences following operation in any of the other types of herniation among adults, and no recurrences following operation in the case of any of the children.

Of the entire series of 304 patients who were operated upon for various types of diaphragmatic hernia, 289 recovered from operation, four of the 289 required a second operation before obtaining relief of symptoms.

DISCUSSION—DR ALBERT O SINGLETON (Galveston, Texas) I was very glad that Doctor Harrington should make his maiden presentation before this organization on diaphragmatic hernia, a subject upon which he is such an outstanding authority. We have been in a quandary relative to the method of repair of some of these difficult herniae. In those about the esophagus in which there is an absence of diaphragm between the esophagus and aorta, a great deal of difficulty has been experienced. In two instances, we have transferred the esophagus further forward in its diaphragmatic penetration and closed the diaphragm behind the esophagus. In two cases of very large hernia in the anterior portion of the diaphragm, we have found it necessary to transplant a large patch of fascia from the thigh, and it has

functioned satisfactorily. We have also experienced a considerable degree of satisfaction in operating upon large diaphragmatic herniae, other than esophageal, through the thoracic approach, finding it much easier than through the abdominal approach. I should be very much pleased if Doctor Harrington would comment upon these points which I have mentioned.

DR J D RIVES (New Orleans, La.) I should like to comment on one of the questions asked by Doctor Singleton. In the case of a very large defect such as he has described, it is quite likely that the best approach would be abdominal, because until exploration has been made it might well be impossible to determine the location and size of the opening in the diaphragm. This would not interfere in any way with the use of the procedure we have proposed for the closure of large defects in the anterior portion of the diaphragm, provided the exploration had been undertaken through a midline or a transrectus incision. I believe that the mobilization of the transversus abdominis would provide a well-vascularized sliding graft that would serve the purpose admirably, and it would be much simpler to do this than it would be to obtain a free graft from some other location.

DR S W HARRINGTON (Rochester, Minn. closing) There is considerable difference of opinion among surgeons concerning the details of the operative technic for diaphragmatic hernia. Limited time did not permit me to discuss many of these technical problems.

Doctor Singleton has asked for discussion of two important technical considerations, namely, the type of approach to be utilized (whether through the thoracic or the abdominal cavity), and the method of closure of esophageal hiatus hernia caused by structural deficiency of the hiatus posteriorly.

I have used both the thoracic and abdominal methods of approach. I prefer the abdominal approach for all herniae through the left hemidiaphragm because when it is used I believe there is less risk of thoracic complications. For herniae through the right hemidiaphragm, I prefer the thoracic approach because the large right lobe of the liver interferes with exposure of the hernial opening. In some types of hernia, such as traumatic hernia and hernia due to congenital structural deficiency of the leaf of the diaphragm, the type of approach may be considered to be the surgeon's choice, because the defect usually is accessible for repair by either method. In the treatment of esophageal hiatus hernia, however, I believe that there are many fundamental advantages in utilization of the abdominal approach, because this type of hernia is sliding and does not enter the pleural cavity, rather, it enters the posterior portion of the mediastinum, behind or lateral to the pericardium.

Removal of the hernial sac or the attachments of the sac to the stomach is one of the important steps in the operative repair of these hernias. The attachments of the hernial sac to the stomach can be exposed only by the abdominal approach. The presence of any associated esophageal lesion, such as traumatic erosion or ulcer, or any injury to the herniated abdominal viscera occurring during the operation, can be recognized readily and treated, if necessary, through this approach.

The type of defective hiatus present can be determined, and hernia due to the posterior structural deficiency of the hiatus can be repaired with less risk of injury to spleen, aorta, and caudal lobe of the liver.

Another important technical consideration in the repair of posterior hiatal hernia, is interruption of the left phrenic nerve for elevation of the diaphragm, so that the opening can be closed around the esophagus at a higher level, since there is usually a moderate shortening or contraction of the esophagus.

- which elevates the cardia of the stomach. It is also important to imbricate several strands of fascia lata into the closure of the posterior margins of the hiatus. This procedure usually insures a very satisfactory and strong closure of this elevated position of the esophagus above the cardia. I have utilized this method of treatment of true congenital short esophagus of moderate degree, in which the surgical problem is not only repair of an enlarged hiatus but also elevation and reconstruction of the diaphragm above the cardia of the stomach.

As to the question of repair of anterior defects of the diaphragm, I may say that I have operated upon four patients who had presented large structural deficiencies of the muscle, and I obtained very satisfactory results by utilizing the fascia of the rectus muscle and reinforcing this with the round ligament of the liver.

BRIEF COMMUNICATION

INTRAMAMMARY HEMANGIOMA*

FRANK WARD SMYTHE, M D

MEMPHIS, TENN

HEMANGIOMATA are not often found in the breast Deaver and McFarland,¹ in 1917, summarized only 13 cases from the literature, dating back to 1837 Menville² found nine cases in 3,000 breast tumors, at the Johns Hopkins Laboratory Bloodgood² said he, personally, had never explored one Johnston,³ during a 15-year period, at the University of Maryland Medical School, noted only one hemangioma in 666 breast tumors In a six-year period, at the Skin and Cancer Unit of the New York Post Graduate Medical School and Hospital, there were 900 benign breast tumors From these, Chohnoky⁴ found nine hemangiomata The records of the last 1,184 breast tumors admitted to the four largest hospitals in Memphis (John Gaston, St Joseph's, Methodist, and Baptist Memorial) show four cases of hemangioma Thus in a total of 5,750 cases, 23 hemangiomata were found, comprising a low percentage (0.04 per cent)

The ratio of those occurring in females to males was 10.5 to one Their ages at the time of examination varied from 11 weeks to 64 years, although most were between 20 and 40

There are two types of breast hemangiomata The capillary and the cavernous The latter are more frequent Most of the tumors are benign, although some are malignant In 1928, Wright⁵ states "Malignant tumors of the blood vascular system, which metastasized to other parts of the body *via* the blood stream, are very rare Less than one dozen of such proved cases have been reported" He separated these into two classes (1) those with an apparently benign structure, and (2) those with a malignant one He, further, believed that the structure in the metastases was always similar to that of the parent tumor Robinson and Castleman⁶ state "that only four authentic cases have been reported Two of these were primarily in the breast" (Boormann's⁷ and Ewing's⁸)

A few cases of metastasizing angiomata of the breast, having a malignant structure, have been reported 11 angiosarcomata, by Schmidt⁹, one similar tumor, by Onsy¹⁰, and a malignant hemangio-endothelioma, by Menville² Ewing⁸ had seen only two metastasizing angiomata, and one of these was from the breast

INSTANCES OF HEMANGIOMA OF THE BREAST OCCURRING IN THE MEMPHIS HOSPITALS

Case 1—White, male, age 40 A hard, smooth, mobile mass, 2 cm in diameter, in lower outer quadrant of left breast No fixation, nipple normal, no drainage, no

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941

regional adenopathy, no pain, no history of trauma *Clinical Impression* Benign solid tumor Operation in 1922 Excision of mass *Pathologic Diagnosis* Benign hemangioma Result, no follow-up

Case 2¹¹—White, female, age 32 A hard, rounded, smooth, mobile mass, 1 cm in diameter, in lower outer quadrant of left breast, no fixation to skin, nipple normal, no discharge, no regional adenopathy, no pain, no trauma *Clinical Impression* Benign solid tumor Operation October 29, 1940 Excision of mass *Pathologic Diagnosis* Benign hemangioma Result, apparently cured to date

Case 3—White, female, age 59 A hard, round, smooth, mobile mass, 2 cm in diameter, in lower outer quadrant of right breast, no fixation to skin, nipple normal, no discharge, no pain, no trauma, no regional adenopathy *Clinical Impression* Benign solid tumor Operation December 8, 1940 Excision of mass *Pathologic Diagnosis* Benign hemangioma Result, apparently cured to date

Case 4—White, female, age 18, seen April 21, 1938 A hard mass, about 6 cm in diameter, in upper outer quadrant of left breast, borders smooth, outline irregular, mobile, no fixation to skin Slightly tender on pressure Nipple was normal No discharge, regional nodes not palpable Present for eight months It was first noticed ten days before a normal menstrual period and a few days after a severe contusion Three months later, after another trauma, the mass increased in size and beneath the skin was a purpuric discoloration On two occasions small purpuric spots had been noticed over the opposite breast However, repeated blood studies, including platelet counts, bleeding and coagulation times showed no evidence of a blood dyscrasia Tourniquet tests were negative *Clinical Impression* Benign mass, probably traumatic fat necrosis Operation April 22, 1938 Cautery excision of mass *Pathologic Diagnosis* (frozen-section) Angioma

On June 18, 1938, appendicectomy for an acute appendicitis

December 19, 1938, apparently a reappearance of tumor in left breast No palpable nodes Roentgenogram of chest clear Roentgenotherapy for reappearance April 19, 1939, apparently cured October 15, 1940, coughing and loss of weight No mass felt in breast, no palpable nodes Roentgenogram of chest did not show metastases No cells were found in sputum Symptoms continued Further study of permanent sections gave the impression of malignancy This was confirmed by Dr James Ewing¹² On November 30, 1940, roentgenograms revealed pulmonary metastases In March, 1941, pulmonary symptoms aggravated Nausea, headache and choked disks pointed to cerebral metastases A downward course continued, in spite of palliative therapy, at Memorial Hospital, New York, and patient died June 21, 1941

Autopsy—Dr F W Stewart¹³

- (1) Capillary angiosarcoma of left breast (no evidence of residual disease)
- (2) Metastatic angiosarcoma to lungs, omentum, mesentery and both ovaries
- (3) Secondary hypoplasia of uterus
- (4) Atrophy and fat replacement of breasts
- (5) Anemia, probably secondary from hemorrhage into disseminated tumor metastases
- (6) Healed surgical wounds of breast and abdomen

Pathologic Diagnosis—Malignant metastasizing capillary angioma Most of the nodules are hemorrhagic and partially necrotic through infarction

Extreme atrophy of endometrium with cystic degeneration of nodes

Marked hyalinization of splenic arterioles (possibly result of radiation)?

This rather complete summary of Case 4, permits three conclusions (1) The frozen-section diagnosis was incorrect (2) The reappearing primary tumor was sensitive to roentgenotherapy (3) The metastases were *via* the blood stream

Diagnosis of these tumors is not easy. They may be diffuse or circumscribed, smooth or irregular in outline, soft or hard. Pain may or may not be present. They may or may not be diminished in size on compression. Some pulsate, others do not. A bruit¹⁴ may be heard. Transillumination is of no definite value. If the lesion is near the surface, there may be some discoloration or an infra-red photograph may prove of value.

Sherry¹⁵ concluded "A unilateral tumor of the breast that increases rapidly in size, decreases in size on compression, only to return rapidly on relaxation, and which may or may not have a bruit or thrill, should be suggestive. When the angiomatous tissue is present in the integument, this only adds to the certainty of the diagnosis."

For the treatment of hemangiomas almost all methods of local attack have been used—injections of perchloride of iron, boiling water and, more recently, sclerosing solutions, electrolysis, actual cautery, roentgenotherapy, radium and surgery.

Operation is the best treatment—for the small tumor, a wide excision, for the large one, a mastectomy. With a very large and extremely vascular hemangioma of the breast, it might be advisable to administer roentgenotherapy before the operation.

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DISCUSSION—DR. BRADLEY L. COLEY (New York, N. Y.) Doctor Smythe has presented a case of extreme rarity. The records of the Memorial Hospital, which contain those of some 20,000 breast cases, show only one

other similar case. In reporting the essential facts of our case, it is hoped that further light may be shed upon this rare condition.

Case Report—An unmarried Jewish female, age 22, was admitted to the Hospital for Special Surgery (formerly the Hospital for Ruptured and Crippled), August, 1925, complaining of a lump in the right breast. Three months previously she had been struck in the right breast by her sister's elbow, a blow had been sustained in the same breast two months prior to that. In the interval elapsing between these two injuries, a lump was noticed which had increased only slightly in size up to the time of admission. There was no history of mammary tumor in the family.

On physical examination, the lower half of the right breast was found to be about twice the size of the normal side. There was a purplish-colored, distinctly localized swelling below the nipple, which represented the encroachment of this mass on the skin. The mass was not so hard as carcinoma. It was thought that the growth was more characteristic of angiosarcoma or endothelioma. Except for the small purplish skin area described above, the rest of the skin was normal in appearance and texture.

Precious Treatment—The patient's first medical adviser carried out local applications for two weeks without improvement. A surgeon was consulted, who made an incision into the mass. Following this operation the patient was assured that the mass would disappear. A month and a half later, the condition being no better, this surgeon advised another operation, which was performed, November 13, 1925, and which, apparently, consisted of removal of the mass by an incision from beneath the breast. A recurrence followed, which was treated by another physician who inserted radium needles, 16, nine needles left in place for two and one-half hours, over an interval of six weeks.

When first seen by me, June 29, 1926, there was an indurated area in the inferior quadrant of the right breast, involving the operative scar. This induration was movable over the chest, but the skin over it was not freely movable. Directly beneath the nipple area it was definitely fixed to the skin. There was no axillary adenopathy. A diagnosis of recurrent angiosarcoma was made, and an immediate radical mastectomy was performed. The raw area on the chest wall resulting from the wide skin excision was allowed to granulate, and it healed in six weeks. Thereafter a total of 16 roentgen ray treatments were administered to the axillae, right and left, in three courses given in July and September, 1926, and in January, 1927.

The pathologic diagnosis was that of malignant angiosarcoma. In December, 1926, a recurrence, about 2 cm in diameter, was noted, and on December 14, 1926, an excision was carried out, and the area was covered with a full-thickness graft taken from the abdomen.

On January 5, 1927, there was roentgenographic evidence of metastasis in the left upper chest. Two months later the patient died, the whole course of the disease being less than two years.

It is interesting to speculate on what the outcome of this disease would have been had a prompt diagnosis been made, and a wide excision—or preferably complete removal of the breast—had been carried out. It is obvious that this tumor was highly malignant and metastasized by the blood stream. It was not apparently influenced by the radiation therapy, although 15 years ago the radiation methods were less effective than those in use to-day.

In retrospect, it would seem that this patient had an incision into the tumor. Then there was a delay of six weeks before excision of the tumor was carried out. Thereafter, a recurrence was treated by the insertion of radium needles which were allowed to remain for two and one-half hours. Finally, an adequate radical surgical procedure was undertaken, but evidently too late, and recurrence and metastases to the lungs eventually ensued.

A plea is made for earlier recognition of the condition and wide surgical removal.

BOOK REVIEW

SKIN GRAFTING BY EARL C PADGETT, M D

THE CHARLES C THOMAS COMPANY have added another monograph to their library of vital and timely books on surgical problems with the contribution by Earl C Padgett on the subject of "Skin Grafting"

The unusually high standard of craftsmanship which the Thomas Company has established is maintained, as was to be expected, and it makes the reading of the book not only easy, but a real inspiration to the younger surgeons of this generation who are beginning to appreciate the necessity for early and massive skin grafting in wounds of the soft tissues

Although skin grafting is one of the oldest of surgical procedures, it was not until comparatively recent years that the surgical profession has employed it as we now know it should be done. In the preface the author rightly gives credit to Blair and Brown for introducing, in 1929, the method of so-called massive split-grafts. This consists in the cutting of a graft considerably thinner than the old full-thickness or Tiersch graft, and somewhat thicker than the type of skin graft formerly used. That the ideal skin graft of such thinness as to secure successful transplantation, and leave the donor's site capable of spontaneous regeneration, can be almost routinely obtained with Padgett's dermatome is one of the outstanding contributions to surgical technic of the present time. With this instrument the inherent human factor and the impossibility of controlling absolutely the level of the hand-held knife are eliminated by the mechanical knife Padgett has devised. He has found that as a rule grafts cut by the hand method, even by the experienced, vary from .008 to .016 inch in thickness, while with the dermatome one can routinely remove a sheet four to eight inches in area and .020 to .024 inch thick, which insures the practical certainty of a take.

In addition, Padgett discusses in this monograph the other factors involved in a successful take, such as proper fixation, tension, hemostasis, pressure, and a clean granulating surface.

Surgeons who have followed Padgett's technic in using this instrument generally agree that the failures to take, which averaged 20 per cent or more of the full-thickness grafts in the past, have been practically eliminated.

It would seem that this is a book that should be in the library of every hospital and of every general surgeon who undertakes the responsibility of traumatic surgery.

WALTER ESTELL LEE, M D

EDITORIAL ADDRESS

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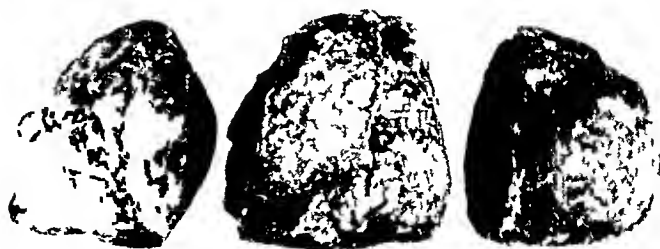
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PLATE I



Postmortem specimen showing under surface of liver. Duodenum and stomach laid open revealing cholecysto enteric fistula. A small stone can be seen projecting through gallbladder fundus into duodenum. Distal to this point there have been replaced, for photographic purposes, three stones which were ultimately found impacted in the lower ileum and causing death from obstruction.



INTESTINAL OBSTRUCTION FROM GALLSTONES¹

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AND

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FROM THE SURGICAL SERVICE OF THE GEORGE F. GIESINGER MEMORIAL HOSPITAL, DANVILLE, PA.

INTESTINAL OBSTRUCTION from gallstones carries one of the highest mortalities among the various causes of acute bowel obstruction. It is likely, at first, to be but partial while the intermittent and none too characteristic symptoms, all too frequently, cause fatal delay in treatment. By the time obstruction becomes complete the patient is, frequently, gravely ill, this being especially true if the obstruction occurs, as it usually does, high in the intestinal tract.

Bartholin,² in 1654, is credited with the first published report of a gallstone perforating into some portion of the intestine. Courvoisier,³ in 1890, analyzed all the then reported cases, 131 in number, his paper being one of the first to focus attention on the problem. A more recent and more comprehensive contribution, made by von Wagner,¹⁸ in 1914, presented an analysis of 334 cases which were found recorded in the available literature.

In reviewing this subject one is impressed by the fact that relatively little has been written regarding it during the past 20 years, the majority of the papers in this time consisting of isolated case reports. It is our purpose to present an analysis of ten personally treated patients and a review of 140 other reported cases, constituting the most significant records of the past two decades, in the hope that, from their collective study, salient points may be emphasized which may prove helpful in a better understanding of gallstone ileus.

Incidence—The occurrence of gallstone obstruction is rare, the incidence given in various reports, in relation to other causes of intestinal obstruction, varying from 1 to 5 per cent. Vick,¹⁷ in an analysis of 6,892 cases of intestinal obstruction seen in 21 London hospitals during the period 1925–1930, refers to gallstones as the etiologic factor in 47 instances, a percentage of 0.68. Dulin and Peterson⁸ stated, in 1939, that in the University of Iowa Hospital they

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9–11, 1941.

had seen ten cases during the preceding ten-year period, accounting for 5.3 per cent of all the cases of intestinal obstruction during that period. A survey recently conducted under the auspices of the British Medical Association revealed gallstones as the cause of intestinal obstruction in less than 1 per cent of all obstruction cases reported from seven London hospitals. Martin,¹² from a questionnaire sent to a number of American surgeons, indicated that, among approximately one-half million operations, there were but 16 cases of intestinal obstruction due to stones, or one among each 30,000 operations.

During the past 15 years the relative incidence in our own hospital has been 4 per cent. In personal communications from other institutions the incidence was given as 1 per cent or lower during the corresponding period of time. These percentages indicate that the incidence is so relatively low that the surgeon may expect to encounter but a few cases during a lifetime, yet Dickson⁷ states that he had had four personal cases in seven years. The author has treated four patients during the past three years and ten in 25 years among 2,720 gallbladder patients admitted to his service (Table I).

TABLE I
INCIDENCE
Geisinger Memorial Hospital
Service of Dr. H. L. Foss

Patients with diseases of gallbladder and biliary ducts	2,720
Patients with intestinal obstruction due to gallstones	10
Incidence of gallstone obstruction among total gallbladder cases	0.3%

The relative ratio of cholelithiasis incidence in the female and male is generally given as five or six to one. It is natural to expect that the ratio should be essentially the same in gallstone ileus. In the collected series studied there were 130 females and 20 males, a ratio of 6.5 to one (Table II). In the study of 150 cases the average age was 62.8 years. The youngest and oldest patients were 31 and 83, respectively, with 55 being in the sixth decade and 41 in the seventh decade (Chart I).

TABLE II
SEX INCIDENCE

Female	130
Male	20
Total	150

Ratio of 6.5 to 1

Mechanism of Perforation—Entrance of gallstones into the intestinal tract may occur in two possible ways. First, through the cystic and common ducts, and, secondly, by means of a fistulous opening between the gallbladder and some portion of the bowel. Probably all gallstones producing obstruction pass by the latter route, and some writers¹⁹ go so far as to say that a gallstone large enough to cause obstruction is never capable of passing through the common duct and must necessarily reach the intestine *via* a cholecysto-enteric fistula. Murphy,¹³ however, cites the incidence of a stone measuring 4.5x2.7

GALLSTONE OBSTRUCTION OF INTESTINE

cm transverse the common duct Cabot³ treated a patient in whom he found, at operation, several diverticula of the duodenum, and he speculated as to whether or not the fistula found between the gallbladder and duodenum had been formed in the base of a diverticulum

The most common procedure is for the stone to perforate through the gallbladder fundus into the duodenum or upper ileum. However, fistulae are reported¹⁴ as having been found connecting the gallbladder and the stomach, the jejunum, the ileum, the colon, and even the urinary bladder. A study of postmortem findings in 42 patients in this study of collected cases revealed the site of the fistula to be between the gallbladder and the duodenum in 41 (Fig 1). In one case there was no fistula, but the cystic and common ducts were dilated sufficiently to have permitted the passage of the stone. Wakefield, Vickers, and Walters,¹⁹ studying operating room and autopsy findings, found that, of 176 cholecysto-enteric fistulae observed at Rochester, the tract occurred between the gallbladder and duodenum in 101, between the gallbladder and colon in 33, and between the gallbladder and stomach in seven. This information, dealing with the site of the fistula, agrees generally with the findings of other authors. The fact that the gallbladder normally lies anterior to the first part of the duodenum and in the closest proximity to it, accounts for the fistulae forming between these two structures in the majority of instances.

The process of perforation begins, naturally, with cholelithiasis followed by ulceration and erosion of the gallbladder wall and fistulous tract formation. Associated pericholecystitis first causes formation of adhesions between the gallbladder and some portion of the intestine, the perforation occurring within a mass of inflammatory tissue which probably accounts for the usual absence of an associated peritonitis. In many instances the gallbladder atrophies after it has emptied itself and has forced the stone into the bowel, as is evidenced by the usual findings of small contracted fibrous gallbladders and the fibrous remnants of a cholecysto-enteric fistula at the time of operation or postmortem examination.

Intestinal obstruction may occur without the gallstone actually entering into the lumen of the intestine. Wakefield, *et al*,¹⁹ cite two instances in which the gallbladder had perforated into the mesentery of the small intestine and

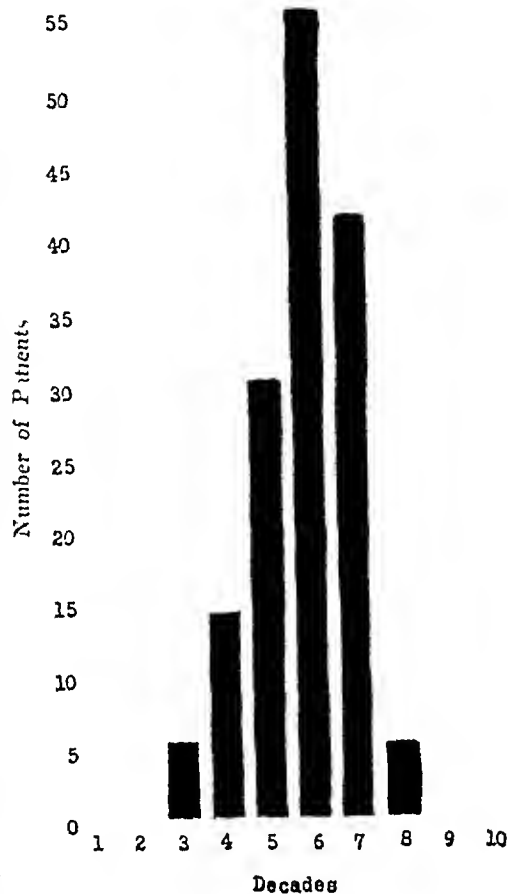


CHART 1—Age incidence

the subsequent tumefaction and abscess formation were sufficient to produce the clinical signs and symptoms of intestinal obstruction. In both cases uneventful recoveries followed operation.



FIG 1—Roentgenogram of stomach and duodenum of patient with cholecystoenteric fistula. Arrow points to projection of opaque medium through fistulous tract, uniting gallbladder and duodenum with gas bubble, immediately above, in gallbladder fundus.

SYMPTOMS AND DIAGNOSIS—The symptoms of intestinal obstruction due to gallstones are less clear-cut than when obstruction results from other and commoner causes. Essentially, the clinical picture is that of ileus, but there are certain features of the symptom complex that may suggest the possibility of a gallstone being the causative factor.

In the majority of cases there is a long and usually intermittent history of gastric distress and epigastric pain. With a few patients there is a definite history of biliary colic. In ten (15 per cent) of the 150 cases analyzed there even had been jaundice. If a patient, particularly a female in the latter decades of life, has symptoms of intestinal obstruction with a past history suggesting gallstones, one should consider the possibility of gallstone obstruction. It is possible, of course, to have similar symptoms in intestinal obstruction from commoner causes, yet, in such instances there should be objective findings such as hernia, weight loss, anemia, and the other characteristic signs of malignancy of the intestinal tract. The latter type of obstruction is likely to be more gradual in its development due to the progressive narrowing of the lumen, whereas gallstone ileus, characteristically, presents intermittent symptoms followed by suddenly occurring complete obstruction. While the opaque enema is of value in ruling out an obstructing neoplasm of the colon, it is of little aid when the obstruction is due to a gallstone, as the majority of obstructions occur in the small intestine. A plain film, however, is of the greatest assistance.

Associated gallbladder disease and the slow development of the obstruction may obscure the picture. To quote Dulin and Peterson⁸ "If there has been previously recognized disease of the gallbladder, the early symptoms of obstruction are easily misinterpreted since the pain, nausea and vomiting resulting from the obstruction are not unlike those of acute biliary colic."

Surprisingly, perforation may occur and not be accompanied by pain or discomfort. However, in the majority of instances there is experienced an acute episode of epigastric pain which the patient reports as being of a somewhat different character from that of previous attacks of gallstone colic which may have been experienced. It is also common to discover no past history that might suggest the presence of chronic cholecystitis or cholelithiasis. As shown in Table III, in this series 23, or 15.3 per cent of the 150 patients,

TABLE III
SIGNIFICANT DATA IN PAST HISTORY OF 150 PATIENTS
Collected Series

	Number of Patients	Percentage
Previously good health	23	15.3%
Pain compatible with gallbladder colic	70	46.6%
Pain compatible with perforation of gallbladder	48	32.0%
History of jaundice	15	10.0%

specifically affirmed that, previous to the onset of the obstruction, they enjoyed the best of health. It is in such cases that it is difficult to make a primary diagnosis. The diagnosis is often delayed because of an indefinite history of intermittent partial obstructive symptoms unassociated with any evidence suggesting gallstone disease. In such cases one might be doubtful as to whether or not the obstructing stone was actually a gallstone or an intestinal enterolith. In the present study, 48 patients, or 32 per cent, gave a definite past history of epigastric pain which, in contrast to previous episodes of biliary colic or epigastric pain and discomfort, could be interpreted as being associated with the process of perforation.

Intestinal Obstruction—After a gallstone perforates the intestine it may pass spontaneously without causing symptoms or there may be intermittent obstructive symptoms which, after a variable time, disappear as the stone is expelled per rectum or, finally, the stone may fail to leave the small bowel and ultimately completely block it. An important factor is the size of the stone. Hennessy¹¹ states that if the calculus is less than two or three cm in dimension, the chances are that it will pass spontaneously. Of von Wagner's¹⁸ 334 accumulated cases, in 93 the stones passed spontaneously. Usually, when the stone reaches the rectum the patient becomes aware of a sense of pressure and has tenesmus and a constant urge to defecate. Occasionally mechanical removal of the stone under an anesthetic becomes necessary.

The usual happening, with a large gallstone, one 25 Mm in diameter or larger, is for it to become wedged in the intestinal tract and cause intermittent partial or complete obstruction. The size of the calculus at the time of the perforation may be of such proportions as to preclude spontaneous passage,

or it may act as a nucleus for the deposition of fecal concretions so that it becomes impossible for peristaltic action to move it further. As the stone becomes arrested in its course the bowel is thrown into a violent spasm and there occur severe colicky attacks associated with nausea and vomiting. As the spasm relaxes the symptoms subside only to recur after variable periods of time as the stone becomes impacted farther along the intestinal tract. If the calculus once passes into the cecum its course is usually uninterrupted unless it is temporarily arrested in the rectum. In the present collected series the location of the obstruction, in 125 of the patients, was in the ileum, and, of this number, 88, or 70.4 per cent, were in the terminal portion, within 12 inches of the ileocecal valve (Table IV).

TABLE IV
LOCATION OF OBSTRUCTING GALLSTONE
Collected Series

Duodenum	6	
Jejunum	14	
Proximal ileum	6	
Middle ileum	31	} + 125 in ileum
Terminal ileum*	88	
Colon	3	
Rectum	2	
	<hr/>	
Total	150	

* Eighty eight or 70 per cent were in the terminal ileum

The higher the point of obstruction the more severe the symptoms. It is only in the late stages that vomiting becomes fecal, which, as Handley¹⁰ has aptly said, "Is not a sign of intestinal obstruction, but rather a herald of approaching death." If the stone is lodged in the duodenum or upper portion of the ileum, abdominal distention is not a prominent feature and visible peristaltic waves and intestinal patterns are rarely present. The fact that gas and feces distal to the site of obstruction may pass spontaneously, or with the aid of an enema, frequently is a factor in the delay in making an early diagnosis. Very rarely is a mass palpable, and in 31 cases in which roentgenologic studies were carried out, in only five, or 16.1 per cent, was a mass demonstrable. Tenderness with rigidity of the abdominal muscles is of little aid, for it is infrequent unless perforation occurs. The leukocyte count and the temperature are generally normal or only moderately elevated. If the obstruction is high and complete, shock and collapse rapidly occur, the outcome becoming fatal unless the condition is promptly recognized and relieved.

Roentgenologic Diagnosis—In a recent and significant contribution by Rigler, Bowman and Noble,¹⁵ the opinion is expressed that by properly conducted roentgenologic examinations "the almost total failure of specific diagnosis in gallstone obstruction with the corresponding high mortality can be corrected to a reasonable high percentage of accurate diagnoses, with an inevitable improvement in the recovery rate." They report the largest series yet presented of cases correctly diagnosed, preoperatively, by roentgenologic studies. The roentgenographic evidence (Fig. 1) on which they depend is

(1) An oral contrast medium in the biliary system, (2) direct visualization of the stone, and (3) the roentgenologic evidence of intestinal obstruction

In recapitulation, the symptoms of intestinal obstruction from gallstones are those of mechanical ileus. There may or may not be a past history of gallbladder disease. The early symptoms of obstruction may simulate biliary colic, but if there has been a previous history of cholelithiasis the patient will usually describe the present episode of pain as being of much different character. At first the obstruction is but partial, but may be absolute, and there is usually characteristic and frequent remissions of symptoms. Abdominal distention, tenderness and rigidity are frequently absent.

In the differential diagnosis one must consider such conditions as (1) Intestinal obstruction due to adhesions, to hernia, to intussusception, or to volvulus, (2) perforated peptic ulcer, (3) mesenteric thrombosis, (4) acute pancreatitis, (5) acute appendicitis, (6) biliary colic, (7) renal colic, and (8) abdominal metastatic infarction. A good maxim to follow is that stated by Gilman⁹: "In absence of an incarcerated or strangulated hernia in elderly persons, in whom previous abdominal surgery has not been performed, one must consider gallstones as well as malignancy as the cause of obstruction."

Obstruction from Multiple Stones—Multiple gallstones are not infrequently encountered in acute bowel obstruction but as a rule only one causes the obstructive symptoms (Plate I). When the obstructing stone is removed and is found to be faceted it indicates that there is, or has been, another gallstone which may still be in the gallbladder or is now in the intestine. A careful and systematic search should always be made when a faceted stone is discovered, and if others are found they should also be removed. One of our own cases, and several found in the literature, illustrate the importance of not overlooking a possible *second* stone at the time of the operation (Table V).

TABLE V
MULTIPLE STONES DISCOVERED AT OPERATION
Collected Series

Site of Obstructing Stone	Site of Second Stone
1 Terminal ileum	Transverse colon
2 Terminal ileum	Transverse colon
3 Terminal ileum	Sigmoid
4 Terminal ileum	Ileocecal valve
5 Terminal ileum	Just proximal to obstructing stone
6 Duodenum	Twelve inches below obstructing stone
7 Middle of ileum	In mass of adhesions beneath liver
8 Jejunum	Cecum
9 Middle of ileum	Just proximal to obstructing stone
10 Terminal ileum	Stone in process of perforating from gallbladder into duodenum

As in our case, postoperative abdominal pain and distention, of a subsequent obstruction, may be misinterpreted and delay in making the diagnosis result in the patient's death. Therefore, if an obstructing stone is faceted the surgeon should make a thorough investigation of the entire ileum especially that segment proximal to the site of the main obstructing stone (Plate I).

Operation—The operation, as a rule, presents but little difficulty. Either a lower midline or a paramedian incision will give good exposure. Spinal is preferred to inhalation anesthesia, which is considered more dangerous since the patients are elderly and often are regurgitating intestinal contents. The obstructing stone is discovered by a systematic palpation of the entire small intestine. The point of obstruction is located either by following down the distended proximal bowel or by following up the lower collapsed portion of the intestine to the site of the obstructing stone. The loop of intestine containing the calculus is withdrawn from the abdomen and packs carefully placed around it so as to isolate it from the abdominal cavity. After applying an intestinal clamp on either side of the stone a longitudinal incision is made along the antimesenteric portion of the intestinal wall over the stone, which is then delivered. Although, in theory, it would be better to remove the stone through an opening made in an adjacent normal intestinal wall, it is the consensus of opinion that it is unwise to attempt to manipulate the stone from the site of its impaction. Most writers favor closing the incision transversely by a double Lambert suture reinforced with interrupted silk rather than longitudinally, since this technic is thought to offer less chance of a subsequent narrowing of the lumen.

Since sulfanilamide crystals have proven efficacious in abdominal surgery, especially where there is actual or potential soiling of the peritoneum, it would be wise to use it locally over the ileotomy site and in the subcutaneous tissues. We have recently used this chemotherapy procedure in various types of intestinal surgery and have been gratified with the results.

Mortality—As patients suffering from an obstructing gallstone are usually elderly, and there is, customarily, a prolonged delay in admitting them to the hospital, it is not surprising that the operative mortality is high. In our group of ten patients the mortality was 50 per cent. The average duration of symptoms in the total mortality-group, prior to operation, was 62 days. Balch¹ has shown that but one of eight patients operated upon after the third day of obstruction survives, and reports that, of nine patients operated upon during the first three days, four will die.

The average duration of complete obstruction before the patients were admitted to the hospital, in our group of our five patients who succumbed, was 52 days. Delay in sending the patients to the hospital was the chief reason for the loss of these patients. Delay is the major factor in producing the high mortality level, and it is only by earlier recognition of the significance of the usually bizarre symptoms of this rare emergency, with earlier diagnosis and more prompt surgical intervention, that we can hope to lower it.

INTESTINAL OBSTRUCTION FROM GALLSTONES

Authors' Series of Ten Cases

Case 1—Hosp No 5809 M B, female, age 47 C C "Gallstones"

History of dull pain in upper abdomen associated with nausea and vomiting at various times during past several years. Two days before admission, onset of dull pain in epigastrium which increased in intensity, nausea and vomiting with distention. Physical

examination revealed epigastric tenderness and rigidity T 95, P 60, R 18 Blood count Hemoglobin, 92 per cent, R B C 7,270,000, W B C 21,600 *Preoperative Diagnosis* Intestinal obstruction of undetermined origin A gallstone 5 cm in diameter was found obstructing the lower third of the ileum

Operation—Ileotomy with removal of stone Gallbladder palpated and found to be small and fibrous, with many surrounding adhesions Patient failed to respond and died six hours afterwards Postmortem examination revealed a fistulous opening between the gallbladder and duodenum The small intestine was distended but there was no evidence of peritonitis The ileotomy suture line was intact

Case 2—Hosp No 11853 J S H, female, age 59 CC "Vomiting"

Had experienced "gas in stomach" for 18 years At irregular intervals had experienced attacks of acute epigastric pain associated with nausea and vomiting Three days before admission had acute abdominal pain with vomiting Enemata ineffectual Physical examination T 99, P 96, R 24 No jaundice Abdomen essentially negative *Preoperative Diagnosis* Intestinal obstruction, cause not determined

Operation—A large impacted gallstone was found obstructing the lower ileum Ileotomy with removal of stone Gallbladder palpated and found to be atrophied and fibrous Uneventful convalescence with discharge on the fifteenth postoperative day

Readmitted 11 years later Chief complaint "Soreness across the abdomen" Had been perfectly well following previous operation until two months ago, when patient began to have irregular episodes of epigastric soreness, which gradually disappeared Was also troubled with "indigestion" and eructations of gas No nausea, vomiting or jaundice Physical examination revealed a well-developed and well-nourished woman of 60, not actually ill No jaundice There was generalized moderate tenderness over the epigastrium without rigidity No abdominal masses palpable *Preoperative Diagnosis* Chronic cholecystitis

Operation—Small, fibrous, atrophic gallbladder containing no bile but having in its fundus one small stone about 0.5 cm in diameter Stone had nearly perforated the gallbladder into the duodenum, to which the gallbladder was firmly attached Gallbladder isolated from duodenum and common duct, which was not enlarged, and removed Discharged on the fourteenth postoperative day

Case 3—Hosp No 39660 J B, female, age 66 CC "Pain in the abdomen"

History of gallbladder colics for 15 years, none for past six months No jaundice Unregulated diabetes mellitus for ten years Present trouble began three days before with onset of right lower abdominal pain Nausea and vomiting, associated with constipation, not relieved by cathartics and enemata Physical examination T 100, P 100, R 20 Abdomen moderately distended No pain or tenderness No masses palpable Blood count Hemoglobin 74 per cent, R B C 5,430,000, W B C 10,150, with an essentially normal differential count Urine 2+ sugar, with no acetone or diacetic acid An abdominal plain film revealed almost complete obstruction in the lower ileum *Preoperative Diagnosis* Intestinal obstruction, cause undetermined

Operation—Large gallstone, 5 cm long, faceted at one end, found wedged in middle portion of ileum Removed Ileum closed with chromic catgut, reinforced with interrupted silk Gallbladder also contained one large stone In spite of supportive measures and regulation of the diabetes the patient became irrational the following day and expired (No autopsy)

Case 4—Hosp No 43879 M C, female, age 67 CC "Constipation"

Prior to present illness patient had enjoyed good health One week before admission experienced an attack of severe epigastric pain associated with nausea and vomiting No bowel movement since onset of illness Enemata were ineffectual Rapidly increasing weakness with abdominal distention Physical examination T 97, P 100, R 28 Patient acutely ill, no jaundice Abdomen markedly distended No masses palpable No tenderness or muscular rigidity Peristalsis audible and moderately active Roentgeno-

gram of abdomen showed the large intestine to be widely distended with gas which stopped abruptly in the lower sigmoid *Preoperative Diagnosis* Intestinal obstruction

Operation—Spinal anesthesia There was no evidence of organic lesion of the large bowel, but there was a large calculus, 4.5×2.5 cm, obstructing the ileum in its mid-portion Ileotomy performed and stone removed Postoperatively, there was a rapid rise in temperature, and the patient expired on the third postoperative day (No autopsy)

Case 5—Hosp No 44049 H T C, male, age 63 CC "Vomiting and constipation"

Past history revealed that five years previously patient had had an attack of severe abdominal pain associated with vomiting and diarrhea Since then has had "indigestion," but no severe pain until present illness Three days before admission, while eating dinner, developed severe abdominal pain which was relieved partially by vomiting The pain and vomiting continued, finally requiring a hypodermic Physical examination T 98, P 100, R 28 Patient obese and acutely ill No abdominal tenderness, but abdomen tympanitic and markedly distended No masses palpable Rectal examination revealed external hemorrhoids and a moderately enlarged prostate Blood count Hemoglobin 90 per cent, RBC 5,590,000, WBC 12,850, with a differential count of 90 neutrophils and ten small lymphocytes *Preoperative Diagnosis* Intestinal obstruction from gallstones?

Operation—Distended loops of small intestine were found proximal to a calculus, 6×3 cm, which was obstructing the lower ileum Ileotomy with the removal of the stone There was slight spilling of intestinal contents In spite of general supportive treatment, which included two transfusions, patient gradually became weaker and expired on the fourth postoperative day The blood NPN, the day before death, was 120 mg (No autopsy)

Case 6—Hosp No 51299 H T C, male, age 63 CC "Stone in rectum"

Eight days previously patient noticed something hard and obstructing in the rectum Family physician had tried unsuccessfully to remove it manually Cathartics produced free movements but mass remained Past history revealed that for eight years patient had had attacks of acute epigastric pain, often requiring morphia Physical examination The abdomen was negative except for some tenderness in the left lower quadrant Satisfactory rectal examination was prohibitive on account of tenderness from previous manipulation Roentgenogram showed no evidence of a mass in the rectum Cholecystogram revealed a nonfunctioning gallbladder The day after admission, while straining at stool, a hard mass was seen and felt at the anal orifice Upon manipulation, a cholesterol stone, 6 cm in diameter, was removed Patient promptly recovered

Case 7—Hosp No 74309B C G, female, age 71 CC "Vomiting and constipation"

Upon admission, nine months previously, a diagnosis of acute cholecystitis and cholelithiasis had been made First attack of epigastric pain occurred three months prior to that time For a year, patient had been somewhat constipated, requiring a frequent laxative Two days before final admission experienced severe pain across the upper abdomen associated with nausea and vomiting There had been no bowel movement for five days Nausea and vomiting continued Repeated enemata were unsuccessful Vomitus fecal Physical examination On admission, patient did not appear acutely ill T 96, P 104, R 20 Obese Abdomen not distended, soft, with tenderness in lower quadrant upon deep palpation A mass was palpable in the left lower quadrant just above the iliac crest, during the initial examination, but never afterwards Hemoglobin 97 per cent, RBC 5,160,000, Color Index 0.9+, WBC 13,400, with a normal differential Abdominal plain film showed evidence of partial intestinal obstruction *Preoperative Diagnosis* Intestinal obstruction from gallstones?

Operation—Spinal anesthesia Upon opening the abdomen, distended coils of the ileum were encountered, which were found to lead to a point of obstruction in the

upper third of the ileum, below which the intestine was collapsed. A calculus, 3.5x3 cm, was found to be the cause of the obstruction, which was removed by enterotomy, with closure of the bowel with running chromic catgut, reinforced with interrupted silk sutures. Upon palpating the gallbladder, a hard nodular mass was found inextricably associated with the first portion of the duodenum. There was also extensive diverticulitis of the sigmoid. Patient developed postoperative bronchopneumonia, which prolonged an otherwise uneventful convalescence.

Case 8—Hosp No 81471. A. L., female, age 71. C. C. "Pain in the left side."

Had been told she had gallbladder disease and had had periodic "biliary drainage" for several years. Past history of several gallbladder attacks. For two weeks before admission patient had been below par. Three days previously she had experienced nausea and vomiting but no pain until day of admission, when pain became acute and located in left lower abdomen. Day before admission there had been two bowel movements. Physical examination revealed an elderly woman who appeared acutely ill and in great distress. T 98, P 92, R 28. Urine 3+ sugar, 1+ diacetic acid and 3+ acetone. There was moderate abdominal distention with marked tenderness in left lower abdomen. Hemoglobin 84 per cent, R B C 4,760,000, W B C 14,800. Abdominal plain film showed no definite evidence of intestinal obstruction. Continued to have intermittent, abdominal, colicky pains but no definite evidences of obstruction were present. *Provisional Diagnosis* Partial intestinal obstruction from neoplasm or adhesions.

Operation—On the fifth day an exploratory celiotomy was carried out under spinal anesthesia. Intestines not distended. Sigmoid explored but nothing found. While the hand was being passed across the upper abdomen a large stone was palpated in the upper ileum. Ileotomy, a faceted stone, 3.5x2 cm, being removed. No other stones were palpable. Postoperative course was uneventful.

Case 9—Hosp No 82666. I. R., female, age 70. C. C. "Vomiting, pain, and constipation."

In good health until onset of anorexia and weight loss seven months previously. Increasing constipation for past four to five months, requiring daily cathartics. No blood or mucus in stools. Four days before admission onset of severe pain across midabdomen, with nausea and vomiting. Cathartics and enemata ineffectual. Physical examination showed an elderly woman, dehydrated and acutely ill. T 96, P 100, R 16, Hemoglobin 104 per cent, R B C 5,590,000, W B C 14,500. Abdomen tympanitic, with generalized tenderness and slight rigidity. No masses palpable. Abdominal roentgenogram on day of admission showed no evidence of intestinal obstruction. Intravenous fluids and supportive treatment instituted. *Preoperative Diagnosis* Intestinal obstruction of unknown etiology.

Operation—Exploratory celiotomy was performed, under spinal anesthesia. Upon opening the abdomen the upper ileum was found to be distended, the remainder of the bowel being collapsed. By following down the distended portion a large, faceted gallstone, 3.7x3x2.5 cm, was found completely blocking the ileum and tightly wedged within it. The stone was readily removed by making a small longitudinal incision in the ileum, which was closed with two running sutures of chromic catgut reinforced with interrupted sutures of silk. Wound closed in usual manner with steel wire reinforcements in the fascia. Two transfusions of 500 cc of citrated blood administered postoperatively. On the fifth postoperative day patient developed abdominal pain and distress. Moderate distention relieved partially by nasal decompression. The temperature became septic, the patient rapidly becoming worse, and expiring on the eighth postoperative day.

Postmortem examination revealed (1) generalized peritonitis, (2) a well-healed fistula between gallbladder and the first portion of the duodenum, (3) ruptured ileotomy sutures, with a second impacted gallstone proximally, (4) pneumonia, right lower lobe, and (5) chronic nephritis.

Case 10—Hosp No 88821 M M, male, age 60 C C "Vomiting of five weeks' duration"

For the previous year patient had experienced distress after meals. Five weeks before admission he began to vomit several hours after eating, which was associated with much belching of gas. The vomiting became more severe, until the patient was unable to retain even fluids. There had been a weight loss of 20 pounds. At no time had there been melena, jaundice or clay-colored stools, or any suggestion of pain in the epigastrium. It was obvious that the patient was suffering from high intestinal obstruction. The roentgenologic report revealed "There is a high-grade obstruction near the pylorus. Peristalsis does not proceed all the way to the pylorus but stops a few centimeters proximal thereto. There is a large retention at six hours." *Roentgenologic Diagnosis* Pyloric obstruction, probably due to carcinoma. *Provisional Preoperative Diagnosis* Pyloric obstruction from carcinoma or possibly from cicatrizing ulcer.

Operation—Spinal anesthesia. "No evidence of carcinoma. Duodenum densely adherent to a small atrophic gallbladder, containing no bile, but four round, faceted stones, each about 2 cm in diameter, which were attempting to perforate into the first portion of the duodenum. The duodenum was separated from the gallbladder with great difficulty because of dense adhesions. About two-thirds of the gallbladder was resected, the gallstones being previously removed." Convalescence followed normally, and the patient was discharged on the fifteenth postoperative day.

SUMMARY

The literature of gallstone ileus during the past two decades has been reviewed, and 140 reported and illustrative cases are analyzed together with ten cases personally treated by the authors. While an exhaustive study of the literature covering the past 20 years was made, it is not contended that 140 represents the total number of cases reported, but, undoubtedly, it includes the majority of them.

The relative incidence of intestinal obstruction from gallstones varies from 1 to 5 per cent. In the series of 150 studied, there were 130 females and 20 males, a ratio of 6.5 to one, which closely corresponds to the relative incidence of cholelithiasis in the two sexes. The majority of patients were in the sixth and seventh decades of life.

A gallstone large enough to cause intestinal obstruction very rarely passes *via* the common duct, the most common route being *via* a fistula between the fundus of the gallbladder and some portion of the duodenum. The sequence of events begins with cholelithiasis, followed by ulceration and erosion of the gallbladder wall, pericholecystitis, and fistulous tract formation.

In the collected series of 150 patients 23, or 15.3 per cent, presented no history suggestive of gallbladder disease, and 48 patients, or 32 per cent, gave a history of epigastric pain which could be interpreted as being associated with the process of perforation. After the stone enters the small intestine it may pass spontaneously, but more often it produces characteristically intermittent obstructive symptoms. The most frequent site for the stone to become lodged is in the terminal portion of the ileum.

Features of the symptom-complex are emphasized in the hope that the entity may be more easily recognized, for it is only by early surgical intervention that the high mortality rate can be lowered. The finding at operation of a faceted stone is emphasized as being indicative of possible multiple stones, the

presence of which should always be ruled out. An abstract of the author's ten personally treated cases is presented.

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DISCUSSION—DR E. VERNON MASTIN (St. Louis, Mo.) I have operated upon five of these cases, in four of them the stone was in the ileum and in one it was in the rectosigmoid. I feel that the high mortality rate can be reduced considerably by simply delivering the dilated obstructed loop of ileum that contains the gallstone, outside of the abdomen as a loop-ileostomy, close the abdomen around the ileum, protect the wound adequately with vaselined gauze and, some hours later, incise the intestine and remove the stone. In this way, we will obviate the risk of peritonitis from leakage of the suture line, which is so prone to occur when a primary suture is employed, if the ileum is markedly distended. There have been no deaths in the three cases in which this procedure was followed, while one, in which I removed the stone and sutured the ileum, died of peritonitis due to leakage.

I have a case to report in which the obstruction was due to a gallstone (Figs. 1 and 2) that was lodged in an old diverticulum of the rectosigmoid. This woman had had severe gallstone colic for years but had refused surgery.

She entered the hospital, in 1931, as an emergency, with generalized peritonitis, the result of a ruptured diverticulum of the rectosigmoid, from which she recovered completely. In 1932 I repaired a large postoperative ventral hernia and at that time exploration of her gallbladder revealed a large stone about 4 cm in diameter. She was admitted again in 1939, with a history of a very severe attack of gallstone colic which began one week previously. She was recovering from this attack when she developed symptoms of in-

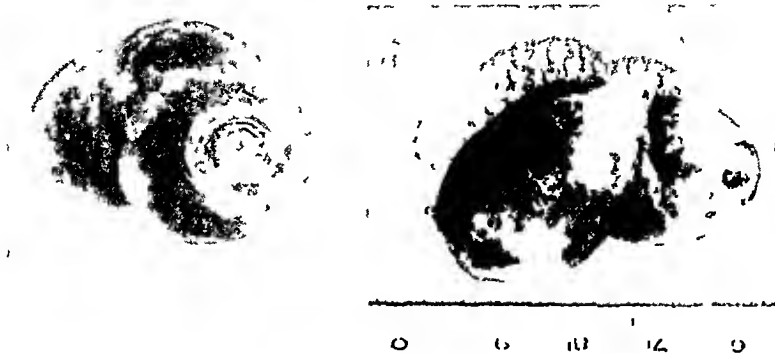


FIG 1

FIG 2

FIGS 1 and 2—Photographs of the gallstone that was removed from the rectum, at the time of operation

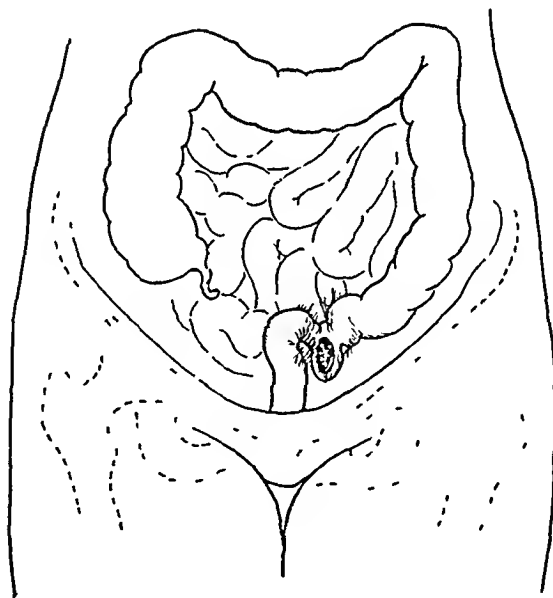


FIG 3—Diagrammatic representation of the anatomic relation of the rectosigmoid diverticulum, containing the indwelling gallstone

testinal obstruction, and exploration revealed a large gallstone impacted in a strictured area of the rectosigmoid (Fig 3). By considerable dissection and manipulation it was possible to free the rectosigmoid and pass the stone through the somewhat strictured portion of the bowel into the rectum, whence it was easily removed by an assistant, with his finger passed through the anus. Exploration of the gallbladder region at this time showed only a mass of dense adhesions between the hepatic flexure of the colon and the under surface of the liver.

Two weeks later a gastro-intestinal series and barium enema failed to show any fistulous communication between the intestine and the gallbladder, and the gallbladder was not visualized by cholecystography (Fig 4). Apparently the cholecystocolic fistula had healed prior to the time the barium enema was given. When last seen a few weeks ago, she stated she had not had any more attacks of gallstone colic.

DR GEORGE G FINNEY (Baltimore, Md) I was interested in Doctor Foss' case because in the last few years, on the ward service of the Women's Hospital, in Baltimore, we have had three cases of obstruction due to gallstones. One of these was of particular interest, because this woman came into the hospital with symptoms of an acute attack five days before. Because of having had two other cases previously, a plain film was taken of the abdomen, and there was a suspicious shadow in the ileum. Both the common duct and the hepatic duct were definitely outlined with air, and, therefore, diagnosis was made of the intestinal obstruction due to gallstone.

She was operated upon and the gallstone was removed. It was located about two feet below Treitz's ligament. She did well for two days and then began to vomit and showed further signs of obstruction. Roentgenograms were again taken, and, sure enough, there was evidence of a second gallstone at a lower level in the ileum. She was operated upon again, and the second stone was removed. That patient lived.

Of the three cases we have had, one has died. This is a relatively high mortality, as indicated by Doctor Foss also.

DR HAROLD L FOSS (Danville, Pa, closing) I can add but little to what has been said, but I was greatly interested in Doctor Mastin's patient who had an obstructing gallstone in a diverticulum. Surely that is a rare condition. Doctor Mastin's suggestion of exteriorization of the loop of ileum containing the obstructing stone may be an answer to the question of how we may decrease the distressingly high mortality of this emergency. The fact that Doctor Mastin's three patients, upon whom he operated by the exteriorization technic, lived, while one upon whom he carried out the usual procedure died, is, of course, a testimony in favor of his suggestion. The stone must be removed, whatever the technic is to be, and the bowel must be firmly closed so there cannot be the slightest possibility of leakage. A non-absorbable suture in the outer coats is most essential, I believe, in this step, and here we have found cotton a particularly satisfactory suture material.



FIG 4—Roentgenogram following a barium enema, 14 days after the gallstone had been removed through the rectum, showing the irregularity of the diverticulum of the sigmoid flexure, in which the gallstone was lodged, and also the hepatic flexure of the colon closely adherent to the undersurface of the liver.

THE SURGICAL ASPECT OF CONGENITAL ABSENCE OF THE GALLBLADDER *

REPORT OF TWO CASES

GEORGE G. FINNEY, M.D., AND JOHN K. OWEN, M.D.

BALTIMORE, MD

RARE CONDITIONS do not always attract the general interest of the medical profession as do the more common ones. There are some conditions which are thought of as rarities only because few cases have been reported. And yet we know that although many surgeons come upon very remarkable and rare cases, the information concerning these cases never gets beyond their office files. When an anomaly, hitherto considered extremely rare, is encountered almost simultaneously by two surgeons working separately in the same city, one begins to doubt if that anomaly is so rare after all. The purpose of this paper is to bring to the attention of surgeons two cases of congenital absence of the gallbladder in adults, and to consider certain practical surgical aspects of the anomaly.

There have been many theories of the causation of congenital absence of the gallbladder. Mauro,¹ in a recent paper, offers what we feel to be a reasonable explanation. As early as the second week of fetal life the hepatic diverticulum develops a ventrocaudal extension, the cavity of which is soon obliterated by proliferation of the epithelium. The extension from which the gallbladder develops is located in the mesenchymatous tissue and remains connected with the hepatic diverticulum by a pedicle from which the cystic duct later develops. The hepatic duct originates from the cranial portion of the hepatic diverticulum and the common bile duct from the caudal portion. During the third fetal week, the liver becomes more separated from the intestine and the bile ducts are thus lengthened and at the same time occluded. The common bile duct reopens during the fourth week and the hepatic duct during the fifth week. Sometime during the sixth week of fetal life, the cavity of the gallbladder reappears. It is almost impossible to determine at the operating table whether absence of a certain portion of the biliary system is due to agenesis or to atresia. This fact is especially true of the gallbladder, which represents the terminal extension and, therefore, may never have existed, or may have undergone secondary involution, on the other hand, if the terminal portion is present, the absence of an intermediate portion can be due only to atresia.

It has been generally accepted that congenital anomalies are apt to be multiple. There are numerous reports of congenital absence of the gallbladder in infants associated with atresia of the bile ducts, according to Bruchsaler² and Ladd,³ this paper is not concerned with such cases. Since

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941

there is a possibility that one of our cases (A O L) represents an hepatic situation of the gallbladder, we must not neglect that condition quoted by Walter,⁴ reported three such cases, in all of which he explored exploratory incision of the liver and found the gallbladder, which contained calculi. In one of his cases, there was profuse hemorrhage which required packing, the patient died on the twelfth postoperative day of diffuse cholangitis and peritonitis. At operation, however, one cannot discover the presence of an intrahepatic gallbladder by any less formidable procedure, since aspiration is done blindly and the bile obtained might well come from one of the bile ducts. Mauro¹ warns against all attempts to perform cholecystectomy in such cases because of the danger of uncontrollable hemorrhage. It is interesting to note that the great majority of intrahepatic gallbladders reported have contained one or more calculi.

Gross⁵ records from the literature 38 cases of congenital absence of the gallbladder, in which there was no other anomaly of the liver or biliary system. He does not include two cases observed by Whipple,⁶ quoted by Sarma,⁷ or the report by Danzis⁸ of one case. Since the appearance of Gross's paper, five other cases have been reported (Mauro,¹ Sarma,⁷ Melville,⁹ Robertson¹⁰), bringing the total to 46.

Case reports of the anomaly have been notably lacking in the essential data. A review of the 11 complete cases reported, including our own, shows that calculi were found in the common bile duct in all, and that the duct was dilated in ten and within the limits of normal in only one. These facts agree with the finding of a proportionately large common bile duct in animals possessing no gallbladder, and also with the common observation that the biliary ducts undergo dilatation following cholecystectomy. The gallbladder fossa may be absent and the quadrate lobe indistinct in outline. Corresponding with the greater incidence of cholelithiasis in females, we find that congenital absence of the gallbladder is twice as common in women as in men. Symptoms usually take the form of a gaseous type of indigestion, with intolerance of fatty foods, and sometimes episodes of sharp lancinating pain in the right upper quadrant referred through the chest to the inferior angle of the right scapula, and occasional jaundice. Thus far, to the best of our knowledge, the diagnosis has never been made preoperatively.

The first case to be presented is that of the senior author (G G F).

Case A O L—A male, age 68, referred by Dr. Louis P. Hamburger, was admitted to the Union Memorial Hospital, March 26, 1941, with the complaint of recurrent attacks of upper right quadrant pain, together with fever, nausea, vomiting, and jaundice of a little more than a year's duration.

Past History—This contains a number of interesting and important facts. At age 17 the patient had a rather severe case of typhoid fever, and at age 32 he had an attack of what was called pleurisy. At age 50 the patient had a siege of dysentery, with blood and mucus in the stools. For the 23-year period from 1910 through 1933, he had suffered with frequent prolonged attacks of hyperacidity, regurgitation, and

sharp epigastric pain, coming on three to four hours after meals. The pain would frequently awaken him at night. During this period he was put on a restricted diet on numerous occasions, and was hospitalized for treatment three separate times. The last occasion was in December, 1933, at which time he spent some three weeks in the Union Memorial Hospital under strict dietary care, with the diagnosis of duodenal ulcer. From this time, the patient had been completely relieved of all symptoms referable to his gastro-intestinal tract until the beginning of his present illness.

Present Illness—In January, 1940, the patient first had an attack of severe right upper quadrant pain which radiated through to the back. This was associated with nausea and vomiting and a moderate degree of fever. The pain was so severe that a hypodermic was required before relief could be obtained. The following day clay-

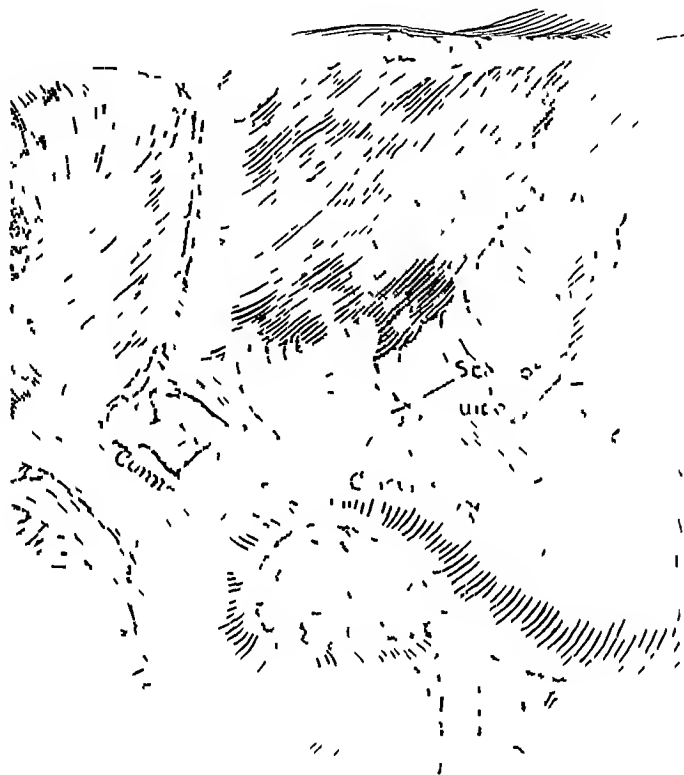


FIG 1—Appearance at operation (Case No. 1)

colored stool was noted and also jaundice. Since this first attack, the patient had had four or five similar episodes, the last one a few days before admission to the hospital.

Physical Examination—The patient was in no apparent distress, but evidenced a moderate icteric tinge to the skin and sclerae. The temperature, pulse, and respirations were within normal limits. Examination of the heart and lungs was normal, and the blood pressure was 144/86. On palpating the abdomen, which was rather large, no mass could be felt and no abnormal resistance or spasm. The liver edge could be felt just below the right costal margin and there was no irregularity or abnormal firmness. Deep pressure in the whole right hypochondrium caused moderate discomfort. In other respects, the examination was normal.

Gallbladder visualization studies were carried out the second day after admission, and the radiologist reported that the gallbladder was not visualized, indicating gallbladder disease probably with cystic duct obstruction. Other laboratory tests showed a relatively normal blood picture—R B C, 4,360,000, W B C, 8,950, Hb 98 per cent, polymorphonuclears, 83 per cent, sedimentation rate 25, and the coagulation time nine and one-half minutes. The prothrombin time was 18 seconds with the control 17

seconds The nonprotein nitrogen was 27, blood sugar 99, and the blood cholesterol 218 mg per cent The icteric index was 300, and the blood Wassermann was negative The urine examination was normal except for the presence of some bile and a few white blood cells in the centrifuged specimen *Postoperative Diagnosis* Cholecystitis with cholelithiasis and possible common duct stone

Operation—March 31, 1940 The abdomen was opened through an upper right rectus incision On entering the peritoneal cavity, the omentum was found lying over the region where the gallbladder should be located On exposing the under surface of the liver, the groove for the gallbladder was seen, but when the entire upper right quadrant was examined carefully, no gallbladder could be found The stomach was normal, but the duodenum showed the scar of an old ulcer on the anterior superior portion There was apparently no obstruction to the pylorus The common duct was then visualized Its identity was ascertained by aspiration from it of a small amount of bile The common duct itself was not unusually distended, being at the upper limits of normal in size When the duct was opened, it was possible to pass a uterine sound up in the hepatic ducts both to the right and to the left When an attempt was made to pass the sound down toward the duodenum, an obstruction was met 3.5 cm below the opening in the duct This obstruction was caused by one small stone and a larger one, 1.5 cm in diameter, somewhat irregular and black in color This latter stone was lodged in the ampulla After its removal, a sound could be passed into the duodenum with ease The duct was thoroughly washed out with normal salt solution and a No. 16 F catheter was placed in the duct for drainage and the duct closed around this with sutures of No. 000 chromic catgut The wound was closed in layers with catgut, except for continuous silk sutures in the skin (Fig. 1)

Postoperative Course—Convalescence was very satisfactory until the fourth postoperative day when a hacking cough developed This became very bothersome, and in spite of medication there were very severe paroxysms even though the chest examination remained negative On the eighth postoperative day, after a hard cough, the patient suffered an almost complete disruption Under pentothal sodium anesthesia, the wound was again closed, through-and-through interrupted silver wire sutures being used Following this procedure the patient's cough for some reason stopped, and the rest of his convalescence was uneventful except for minor difficulties in voiding at times He was discharged from the hospital May 12, 1940, with his wound healed, and ate a normal diet without any discomfort He was last seen a few weeks ago, and showed only a small weakness at the upper end of his incision as a result of his disruption, but asymptomatic

The second case is that of the junior author (J. K. O.)

Case C. A. G.—White, female, age 69, was admitted to the Hospital for the Women of Maryland, February 5, 1941, complaining of a dull ache in the right upper quadrant following exertion The pain was steady and was accompanied by dyspnea, usually, but not always, the pain was relieved by resting or by the administration of spirits of niter The pain often extended to the substernal region and sometimes radiated through the chest to the inferior angle of the right scapula Attacks lasted from a few minutes to several hours and were often associated with nausea and vomiting and sometimes chills but never jaundice She also noted ankle edema in the evening The pain had never radiated to the left shoulder or down the left arm At the time of an attack she complained of palpitation She avoided greasy foods because of postprandial distress in the form of gaseous eructations and heartburn All the foregoing symptoms had been recurring for two years prior to admission She was moderately constipated and thought she had passed acholic stools There has been no weight-loss There was no history of typhoid fever

Physical Examination—Blood pressure varied between 186/80 and 150/40 The patient was orthopneic and required three pillows There was pitting edema of both lower legs The lungs were clear to percussion and auscultation The heart was not

enlarged to percussion and sounds were clear, without murmurs. An occasional ventricular extrasystole was heard. There was moderate tenderness over the entire right upper abdominal quadrant, but no spasm.

Special Studies—A gallbladder roentgenologic series was done twice, without visualization of the gallbladder. Electrocardiograms showed evidence of myocardial disease. Urine negative. Hemoglobin was 82 per cent (Sahli), fasting blood sugar 85 mg per cent. Blood nonprotein nitrogen 30 mg per cent. Blood Wassermann negative. The van den Bergh test showed delayed reaction.

Preoperative Course—It was felt that the patient, unquestionably, had heart disease, and biliary disease as well. The plan was to treat her biliary disease conservatively and to concentrate on her cardiac pathology, but, on February 9, 1941, she had an attack of severe pain in the right upper quadrant, there was marked tenderness and

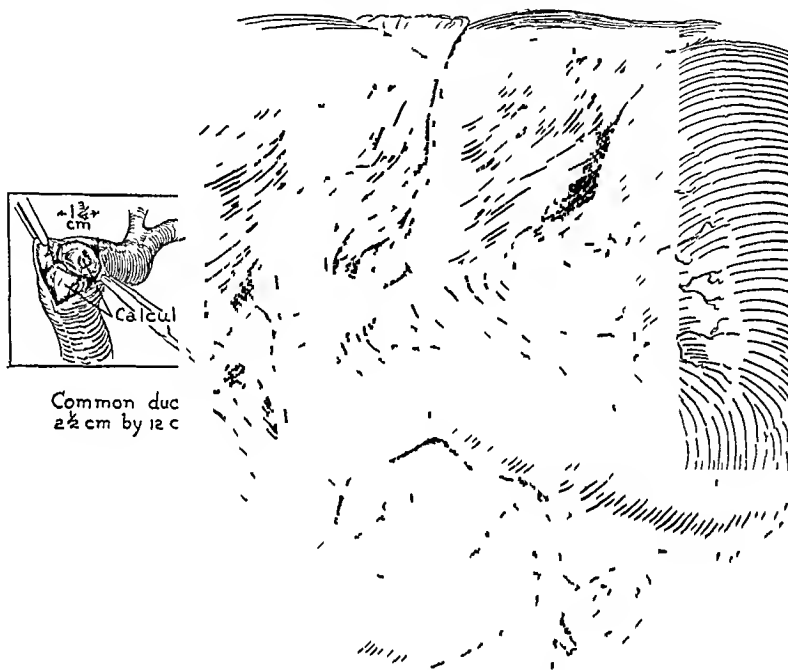


FIG 2—Appearance at operation (Case No 2)

moderate spasm over the region, and the temperature rose to 103.2° F by mouth. She pleaded for some form of relief, and we all agreed that operative intervention was indicated, even though it involved considerable risk in the face of obvious heart disease. Therefore, on February 10, 1941, a course of aminophylline gr 15 tid and coramine gtt 15 tid was begun. She had still another attack on February 12, 1941.

Operation—February 12, 1941. The abdomen was opened through a right subcostal approach, and the liver was found enlarged to three fingers breadth below the costal arch, it had the classic appearance of chronic passive congestion. Lying in a very shallow groove of the liver, where, ordinarily, the gallbladder fossa is located, was a mass of tissue surrounded by light adhesions and containing two calculi. The adherent structure was dissected free and was found to be a considerably dilated common bile duct. There was no evidence anywhere of a vestige of the gallbladder or cystic duct. The common bile duct was incised and two calculi, measuring 1.5 cm in diameter, were removed. Thorough exploration of the dilated hepatic ducts and common bile duct was carried out with sounds and a catheter, and no other calculi were encountered. The quadrate lobe was indefinite in outline. The pancreas felt normal throughout. The stomach, pylorus, and duodenum all appeared normal. The incision into the common bile duct was closed about rubber tubing, interrupted sutures of medium silk being used. One cigarette drain was placed through the foramen of Winslow into the

CONGENITAL ABSENCE OF GALLBLADDER

lesser peritoneal cavity and another to the site of the choledochostomy. The operation was prolonged by efforts at exploration, and the patient left the operating room in only fair condition.

Postoperative Course—Hypodermoclysis in both thighs was begun the evening of the operation. The next day the pulse became weak and rapid and the patient became slightly cyanotic. She was given oxygen, which did not greatly improve her color. Her temperature rose during the day and at noon was 103.4° F by rectum. She was given the usual stimulants and even artificial respiration, but she died that afternoon, some 24 hours following operation.

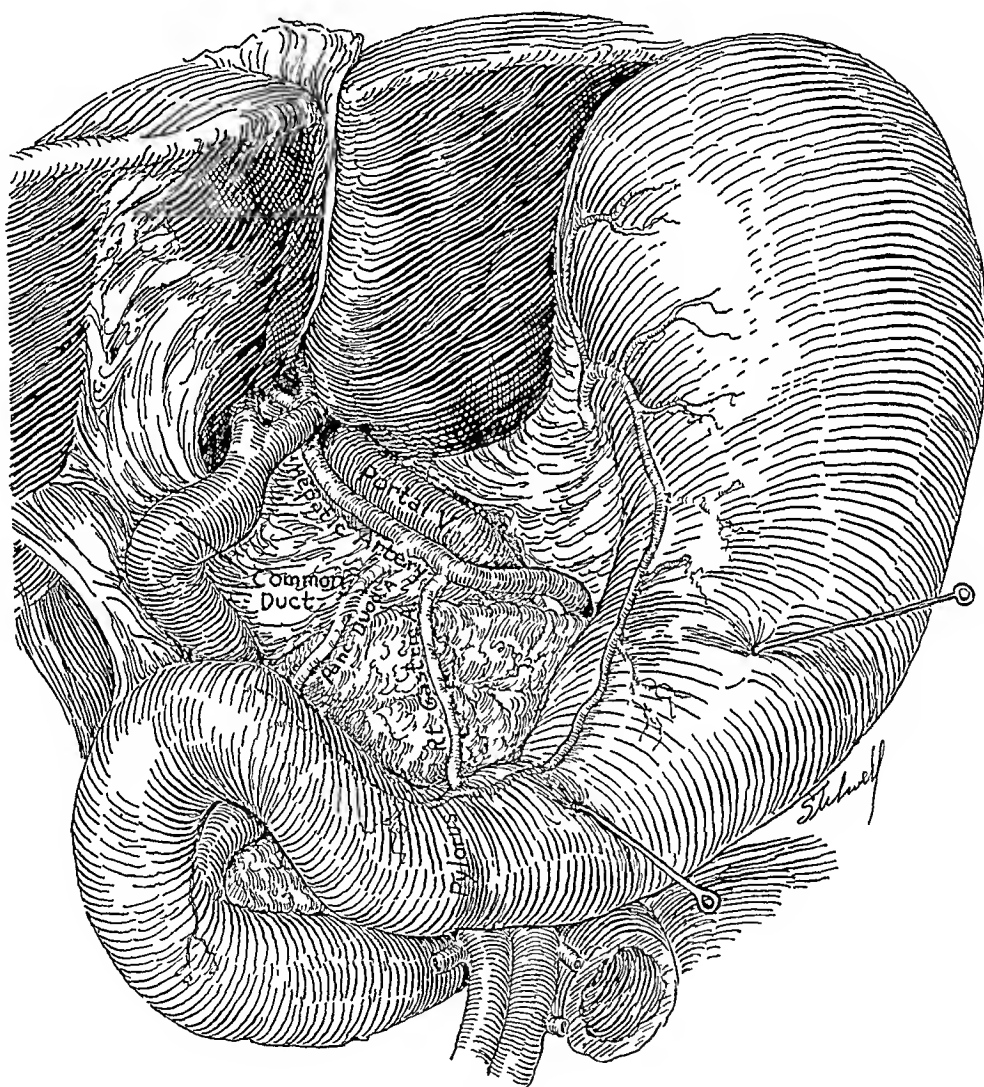


FIG 3—Appearance at autopsy after the stomach had been rolled downward. Note unusual relative position of hepatic artery and portal vein.

Partial Autopsy—Rigor mortis had not set in. There was pitting edema of both lower legs. The intestine was moderately distended. There was no evidence of bile leakage. The liver still showed chronic passive congestion. The common bile duct measured 2 cm in its greatest diameter. The liver was sectioned in every plane, and there was no sign of an intrahepatic gallbladder. The biliary duct system was carefully dissected and no evidence was found of a vestige of the cystic duct or gallbladder. The coronary vessels were sclerotic but there was no infarction. There was considerable calcification of the aortic arch. Pancreas, stomach, pylorus, and duodenum were grossly normal. Histologic study showed midzone necrosis of liver lobules with shadow-type of cell, together with many leukocytes. The large veins were engorged and contained many leukocytes. Pancreas and myocardium were normal. *Pathologic Diag-*

noses Congenital absence of the gallbladder Cholangitis, acute, with cholelithiasis
Arteriosclerotic heart disease, with hypertension

There are a number of interesting surgical considerations that arise when we study the two cases herewith reported, and other similar ones collected from the literature. In the first place, when abdominal exploration is carried out in a patient with suspected gallbladder disease and no gallbladder can be found, there is the possibility of an intrahepatic gallbladder, as well as calculi in the biliary ducts. Exploration of the ducts should then be carried out, and if no calculi are found, in spite of a definite history of biliary disease, one is justified in making a reasonable attempt to find whether there is an intrahepatic gallbladder. In one of our cases, we are sure there was no intrahepatic gallbladder since the patient did not survive because of her heart condition and complete section of the liver was possible. In the other case, however, because of the fact that, on thorough exploration, there was no evidence of an intrahepatic gallbladder, as far as could be determined, and also because the patient has been completely relieved of his symptoms following the removal of the stones from the common duct, it seems quite presumptive that there was congenital absence of the gallbladder. Unfortunately, in many case reports of congenital absence of the gallbladder, the data are not given in enough detail to permit definite conclusions to be drawn. It is true, however, that in practically all the cases where the common duct was much larger than normal, stones were present.

SUMMARY

We have presented two cases of congenital absence of the gallbladder together with 46 similar cases collected from the literature after a rather exhaustive search. We have included only those cases in which no other pathologic condition was present, and have, therefore, left out a large number of cases where there was either complete or partial absence of the common and hepatic ducts as well. Some consideration has been given to the cause of absence of the gallbladder from the embryologic standpoint, and a few of the surgical aspects are discussed.

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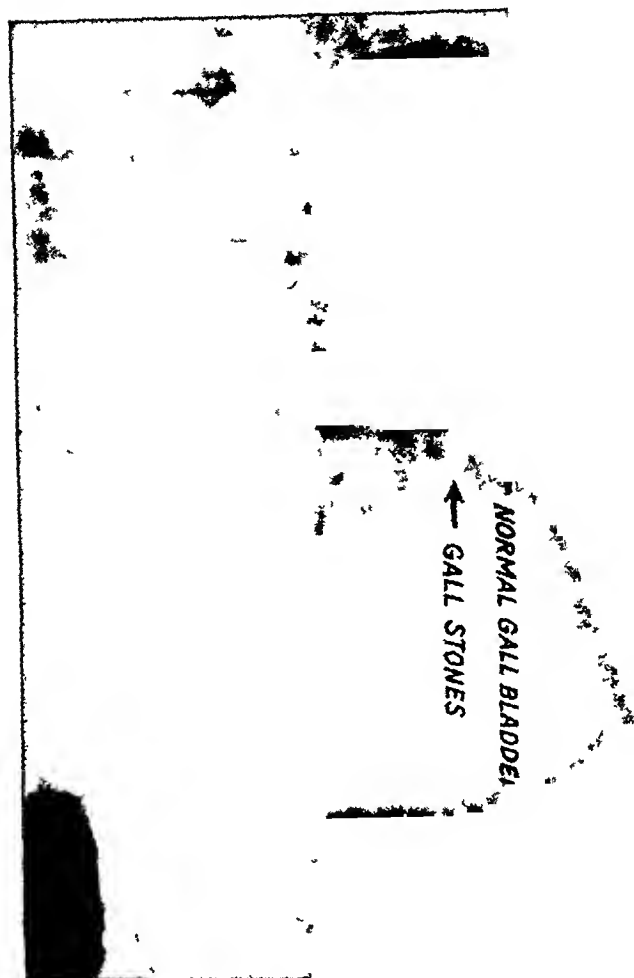


FIG 1—Roentgenogram showing a duplicate of the gallbladder—one containing calculi, the other apparently containing dye only

DISCUSSION—DR HUGH TROUT (Roanoke, Va) In 1933, we[†] reported a case of duplication of the gallbladder. At that time we looked up the literature and found there had been 34 cases reported to date. A subsequent review shows that since then 18 additional cases have been reported. So far as I know the literature does not reveal a case where the diagnosis was made roentgenologically prior to operation. We were fortunate enough to have one such case (Figs 1 and 2).

At operation, the two gallbladders were removed. Each was complete, with cystic duct, the cystic ducts joined just before entrance into the common duct. Boyden[‡] demonstrated that this was the most frequent type

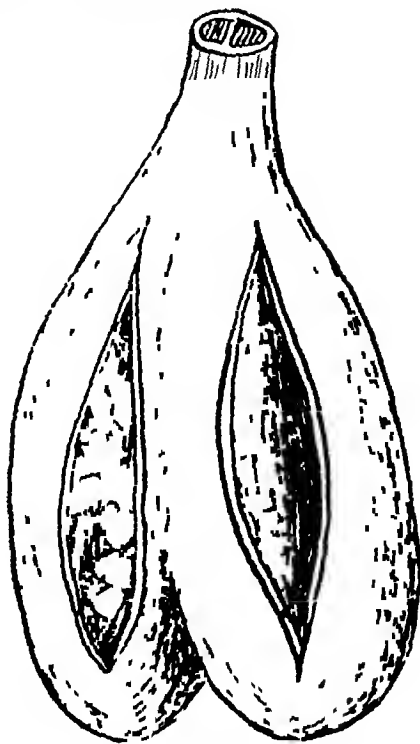


FIG 2—Graphic representation of roentgenographic interpretation of duplication of the gallbladder. (The artist has transposed the roentgenographic shadows.)

* Slaughter and Trout. Amer Jour Surg, 19, 124-125, January, 1933.

‡ Boyden. Amer Jour Anat, 38, 177, November, 1926.

of cystic duct relationship in the duplication of the gallbladder. Boyden, also after a study of 19,000 autopsies done in several anatomic laboratories, showed five cases of duplication of the gallbladder, an incidence of one in 4,000. I think this condition perhaps is more frequent than has been supposed. A number of lower animals, especially cats, have been found to have duplication and accessory gallbladders. In fact, as many as four gallbladders have been found in one cat.

ANATOMY OF THE ATTACHMENTS OF THE DIAPHRAGM THEIR RELATION TO THE PROBLEMS OF THE SURGERY OF DIAPHRAGMATIC HERNIA^{*}

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NUMEROUS STUDIES of the etiology, diagnosis, and treatment of diaphragmatic hernia have appeared in recent years,^{7, 8, 10, 13, 17, 21, 22} and in several of them the literature has been fully reviewed. Nothing would be gained at this time by another review of that type, consequently, the scope of this contribution is limited to an account of some new observations on the anatomy of the attachments of the diaphragm, comments on the surgical significance of these observations, and the report of two methods that we think useful in the repair of unusually large defects in this septum, regardless of their etiology.

Anatomy—The usual description of the peripheral attachments or origins of the diaphragm^{5, 9, 20, 24} may be summarized as follows: (1) The anterior or sternal portion is attached to the xiphoid process and the adjacent aponeurosis of the transversus abdominis or to a tendinous arch extending from the xiphoid to the cartilages of the fifth and sixth ribs (Fig 1 a). (2) The lateral or costal portion arises from the posterior surfaces of the cartilages of the seventh, eighth, and ninth ribs and from the osseous extremities of the tenth, eleventh, and twelfth ribs. The segment attaching to the seventh, eighth, and ninth ribs is said to interdigitate with the transversus abdominis, and the more posterior portion is described as arising in part from tendinous arches that bridge the origins of the transversus abdominis in the last three interspaces (Fig 1 a). (3) The posterior or lumbar segment (Fig 1 b) arises by means of three pairs of crura from the bodies and transverse processes of the upper lumbar vertebrae and from the arcuate ligaments. Only the lateral crus concerns us in this discussion. It is said to be attached to the bodies of the first and second lumbar vertebrae and to the medial and lateral lumbocostal arches (arcuate ligaments) which are described as fibrous condensations of the fascia covering the psoas and quadratus lumborum muscles. The medial arch (internal arcuate ligament) is said to be attached at one extremity to the body of the second lumbar vertebra and at the other to the corresponding transverse process. It bridges the bellies of the psoas muscles. The lateral arch (external arcuate ligament) bridges the belly of the quadratus lumborum and is said to be attached at its medial end to the tip of the second lumbar transverse process and at its lateral end usually to the tip of the twelfth rib.

Our artist, Mr W Blanks Stewart, found, when he attempted to make drawings of the diaphragm from cadaveric dissections for Doctors Baker

^{*} Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941.

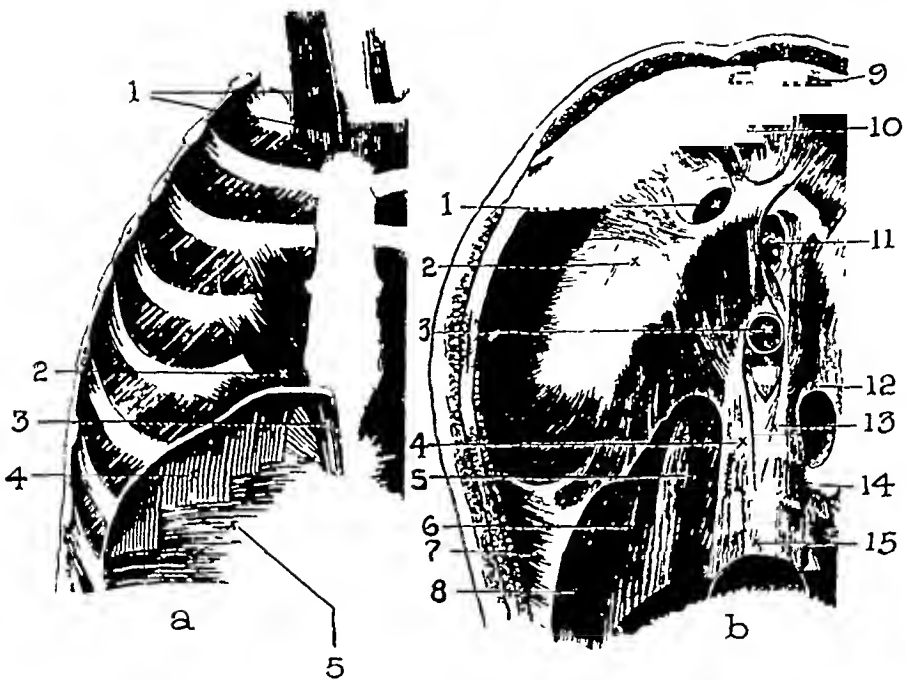


FIG 1.—Textbook illustration of anatomy of diaphragm (Modified from Morris *Human Anatomy*)

- (a)
- (1) Sternothymoid
 - (2) Transversus thoracis
 - (3) Sternal origin of diaphragm
 - (4) Costal origin of diaphragm
- (b)
- (1) Opening for vena cava inferior
 - (2) Right division of tendon
 - (3) Aorta
 - (4) Right crus
 - (5) Psoas minor
 - (6) Psoas major
 - (7) Transversus abdominis
 - (8) Quadratus lumborum
 - (9) Sternal origin
 - (10) Middle division of tendon
 - (11) Esophagus
 - (12) Medial lumbocostal arch
 - (13) Left crus
 - (14) Transverse process of second lumbar vertebra
 - (15) Fourth lumbar vertebra

and Burns, that he could not harmonize this description with his specimens. This fact led Doctor Baker to undertake a series of dissections of the diaphragmatic attachments in human cadavers. These dissections revealed the fact that while the above description is approximately correct insofar as the ultimate points of bony attachment of the diaphragm are concerned, it fails to give a true picture of the attachments of the costal segment and of the lateral portion of the lumbar segment in their relations to the transversus abdominis muscle and to the lumbar fascia. We find that the attachments of the costal portion of the diaphragm and those of the transversus abdominis to the costal cartilages and ribs (Fig 2 a) are so intimately blended anteriorly (in the region of the seventh, eighth, and ninth cartilages) that they are inseparable, and that posteriorly (tenth, eleventh, and twelfth ribs) the two muscles are united by a common aponeurosis which becomes progressively wider as it is traced backward to the lateral margin of the quadratus lum-

boium where it blends with the lumbodorsal fascia (Fig 2 b) This common aponeurosis attaches to the tips of the tenth and eleventh ribs but only indirectly to the twelfth Medial to the tip of the twelfth rib, it blends with the fascia that bridges the triangular defect in the musculature of the

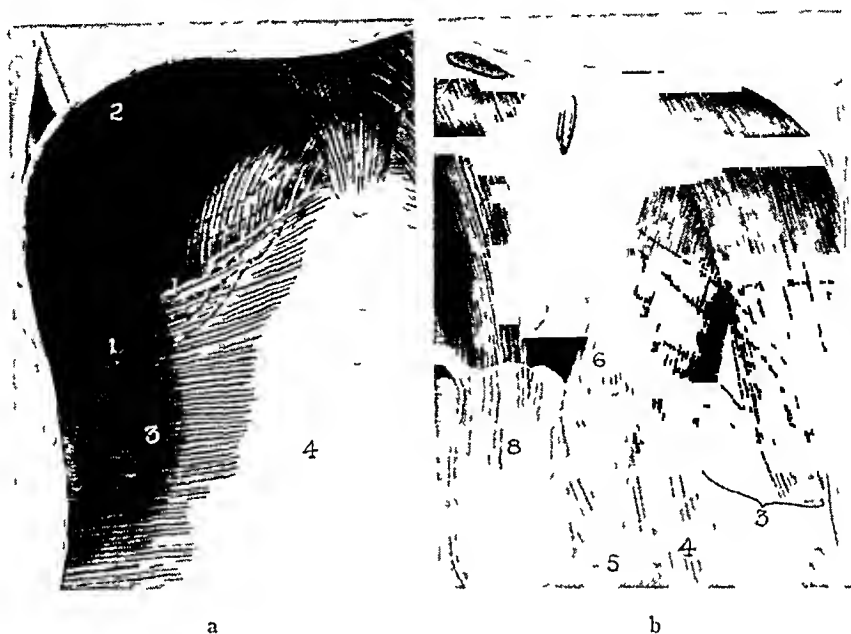


FIG 2—Attachments of the diaphragm as revealed by authors' dissections

(a)

- (1) Common aponeurosis and transversus abdominis attached to posterior surfaces of costal cartilages and tips of ribs
- (2) Anterolateral portion of the costal segment of the diaphragm
- (3) Transversus abdominis
- (4) Posterior sheath of rectus abdominis

(b)

- (1) Posterolateral portion of costal segment of diaphragm
- (2) Tip of twelfth rib
- (3) Fusion of the common aponeurosis of the transversus abdominis and the diaphragm with the lumbodorsal fascia
- (4) Quadratus lumborum
- (5) Psoas muscles
- (6) and (7) Condensations of the anterior layer of the lumbodorsal fascia giving attachment to the diaphragm (medial and lateral lumbocostal arches)
- (8) Prevertebral fascia

diaphragm that represents the former site of the pleuroperitoneal hiatus (foramen of Bochdalek) In effect, therefore, the diaphragm and the transversus abdominis are continuous with each other, a fact which can be readily and graphically demonstrated by freeing their attachments to the costal arch, thus converting the two muscles and their common aponeurosis into a continuous fibromuscular sheet which together with the rectus sheath and the lumbar fascia enclose the abdominal cavity (Fig 4)

Medial to the former site of the hiatus pleuroperitonealis is the lateral margin of the lumbar segment of the diaphragm (Fig 2 b) Dissection of its attachments reveals a state of affairs quite similar to that seen in the costal portion The arcuate ligaments, to which the lateral crus attaches, are found to be simply condensations of the lumbopsoas fascia attaching only indirectly, through the lumbodorsal fascia, to the tip of the twelfth rib and the transverse process of the second lumbar vertebra The lateral attachment of the lateral crus is, therefore, really to that layer of the lumbar fascia which covers the

anterior surfaces of the quadratus lumborum and psoas muscles (Fig 2 b) and Fig 3) That it is actually continuous with this fascia is amply attested by the fact that muscle fibers have actually been seen to extend from the diaphragm through the arcuate ligaments and into this fascia. In effect, therefore, the diaphragm is continuous with the inner fibromuscular layer of the abdominal wall.

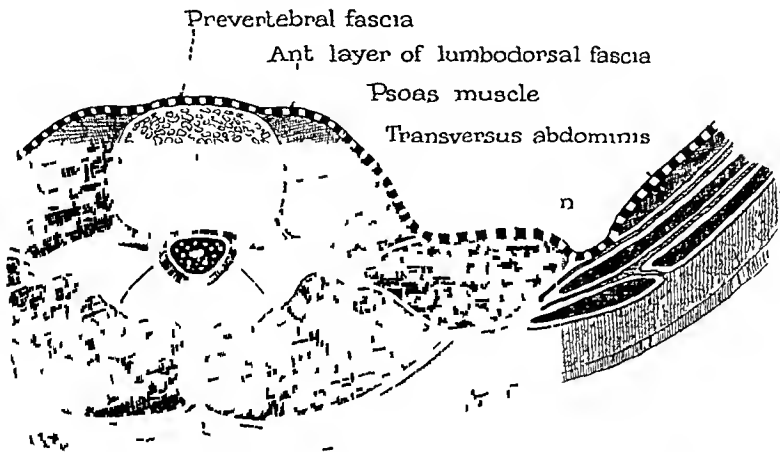


FIG 3—Cross section below the level of the attachment of the diaphragm showing the anterior layer of the lumbodorsal fascia which is continuous with the lateral portion of the lumbar segment of the diaphragm. Note that this layer is attached only indirectly to the transverse process of the vertebra.

Since making this study we have been interested to find that Sir Arthur Keith¹⁴ has observed the continuity of the diaphragm with the transversus abdominis and posterior lamina of the rectus sheath in the developmental stage, and that, in 1676, Caspar Bartholin, son of Thomas,² described the diaphragm and the transversus abdominis muscles combined as a trigastic muscle.

Embryology—It is very tempting, after studying these dissections, to think of the diaphragm as representing the inner layer of the thoracic portion of the coelomic cavity stripped from the surface and forced downward by the descent of the thoracic viscera, but unfortunately this is not in accord with the known facts. The most probable explanation is as follows. The diaphragm, which is a late development in the evolutionary process, being found only in mammals, is formed from three different sources, two of which are paired. The three parts develop independently and on different time schedules: (1) The anteromedial portion develops from the transverse septum, (2) the posterolateral portions from the pleuroperitoneal membranes, and (3) the lumbar portion from the dorsal mesogastrium. At about the seventh or eighth week of fetal life, these segments fuse to form a single fibrous septum which later is converted partially into muscle. Shortly after this has taken place, the liver grows so rapidly that it expands the upper abdomen faster than the diaphragm can grow. Consequently, a portion of the inner wall of the abdominal cavity is pulled inward to become the peripheral margin of the diaphragm^{1, 23} (Fig 5). This probably accounts for the continuity of the diaphragm with the inner layer of the abdominal wall.

Diaphragmatic Hernia—In view of the complex origin of the diaphragm, it is not surprising that we find that congenital openings not infrequently occur. A review of the reported defects is beyond the scope of this paper. For our purposes, it is sufficient to say that any part or all of one leaf of the

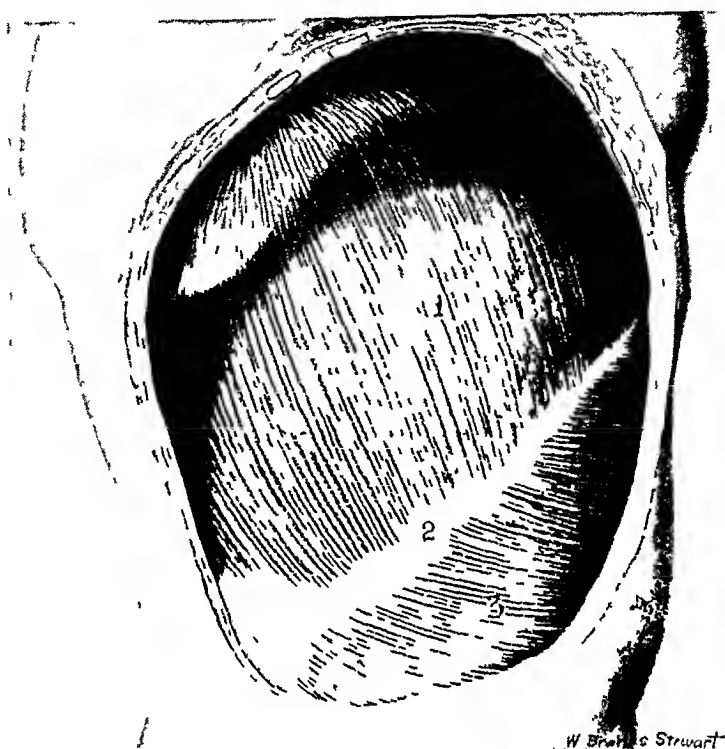


FIG 4—The right side of the diaphragm, the transversus abdominis, and their common aponeurosis exposed by removal of parts of the thoracic and abdominal walls

- (1) Diaphragm
- (2) Common aponeurosis of diaphragm and transversus abdominis
- (3) Transversus abdominis

diaphragm may be found missing. Very large defects are most common in the posterior portion and on the left side. Complete bilateral absence of the lumbar segments has been reported.⁸ Infection and trauma may also, on occasion, cause very large defects.

Most openings in the diaphragm may be closed by simple suture without great tension (especially if the phrenic nerve is crushed as a preliminary step) because the convexity of the diaphragm affords a considerable amount of slack, but when the defect is very large some means of supplementing the available amount of tissue or of diminishing the anteroposterior diameter of the thorax may be necessary. This is especially true when the hiatus is a marginal one, as in hernia through a persistent pleuroperitoneal foramen. Free fascial grafts may be used but are subject to the disadvantage that they cannot be placed in a satisfactorily vascular bed. It seems desirable, therefore, to use some form of sliding or pedunculated flap. When the common attachments of the transversus abdominis and the diaphragm have been dissected from their costal attachments, one is immediately impressed by the fact that the diaphragm has been augmented by an additional segment equal

to almost one-half its total area (Fig 4), and that the entire structure can easily be drawn down below the costal arch, even in the fixed cadaver. The following procedure (which has been performed only on the cadaver) is, therefore, proposed for very large defects in the anterior and anterolateral portions of the diaphragm.

A subcostal incision is made about one inch below the costal arch, extending from the lateral margin of the rectus sheath to about the tip of the tenth or eleventh rib. This incision is carried down through the external and internal oblique muscles, exposing the transversus abdominis. The in-

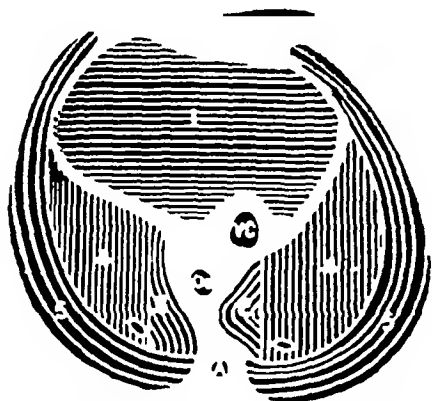


FIG 5.—Diagram showing the origin of the diaphragm (after Broman). (1) Septum transversum, (2, 3) derivatives of mesentery, (4, 4) derivatives of pleuroperitoneal membrane, (5, 5) parts derived from the body walls, A, aorta, Oe, esophagus, VC, inferior vena cava.

ternal oblique is then separated from the anterior surface of the transversus anteromedially to the attachment of the latter to the posterior rectus sheath. The costal arch is retracted anteriorly and superiorly so that, by blunt dissection, the common attachment of the transversus abdominis and the diaphragm is exposed. By careful sharp dissection with the blade of the knife directed toward the ribs, this aponeurosis is dissected from its costochondral attachment for the full length of the incision (Fig 6 B). The pleural cavity is usually entered during this procedure, and

this opening should also be enlarged to the full length of the incision, after which it is possible to pull the diaphragm down well below the costal arch. The contents of the hernia are then fully exposed, making the freeing of adhesions and the replacement of the viscera in the abdominal cavity comparatively easy. The defect can then be closed with adequate overlapping of the edges and without tension even if as much as one-third of the leaf is absent (Fig 6 C and D). Part of the transversus abdominis now slides into the chest cavity and becomes a part of the diaphragm. The anterior surface of the transversus abdominis is then sutured securely to the costal margin, thus closing the thoracic cavity (Fig 7). If, after this has been done, the abdominal cavity should be too much reduced in capacity, the transversus abdominis may be detached from the posterior sheath of the rectus muscle, and in addition, if necessary, it may be divided by an incision parallel to the costal arch and well below the skin incision, thus permitting it to slide freely into the thoracic cavity without reducing the capacity of the abdomen. If the peritoneum should be opened during this maneuver, either by accident or by design, the resulting defect can readily be covered with the omentum or, on the right side, with the falciform ligament. It is probable that more than one-half the area of one leaf of the diaphragm can be supplied by this method.

Large marginal defects rarely occur in the anterior portion of the

diaphragm, but it seems to us that this approach would provide an ideal method of closure for such cases

Very large defects in the diaphragm are much more common in its posterior than in its anterior portion, largely because of the frequency of

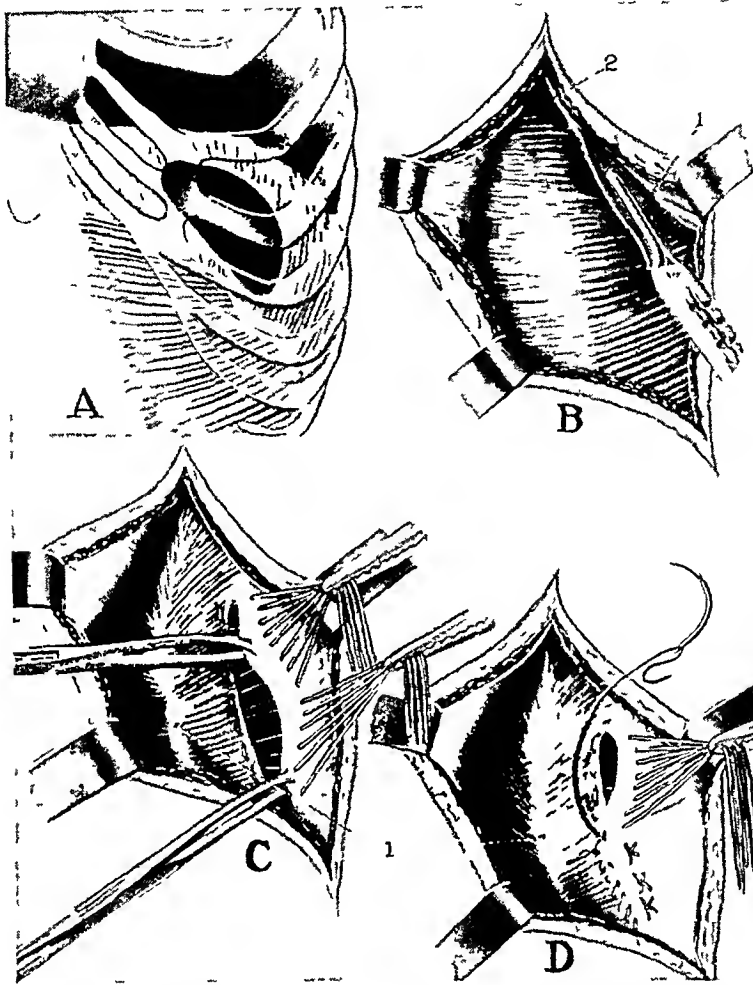


FIG 6—Operative procedure proposed for large defects in the anterior portion of the diaphragm
A Large defect in anterior portion of diaphragm
B Common attachment of transversus abdominis and diaphragm being dissected from its costal attachment
(1) Costal arch retracted upward
(2) Common aponeurosis of the transversus abdominis and diaphragm
C and D Defect in diaphragm pulled down below costal arch and closed with overlapping of the edges
(1) Common aponeurosis of transversus abdominis and diaphragm

persistence of the pleuroperitoneal hiatus, but the procedure described above is not suitable for such cases, for the lumbar attachments of the diaphragm are quite inaccessible from an anterior transthoracic incision. A posterior approach embodying the same principles is not practicable, for the lumbar fascia cannot be mobilized as can the transversus abdominis. However, a suitable sheet of muscle to close the defect can be obtained from the latissimus dorsi, as was done in the following case

Case Report—B. M., white, female, age 19, presented herself to Dr. Frank Brock, February 23, 1936, complaining of attacks of pain in the epigastrium and right upper

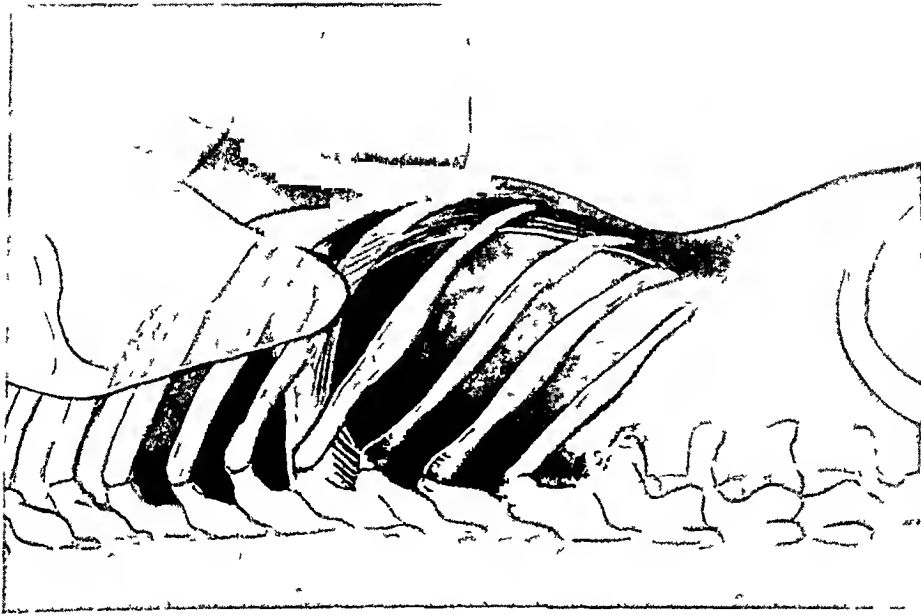


FIG 8—Case of Miss B. M. Complete absence of the posterior lateral segment of the right leaf of the diaphragm

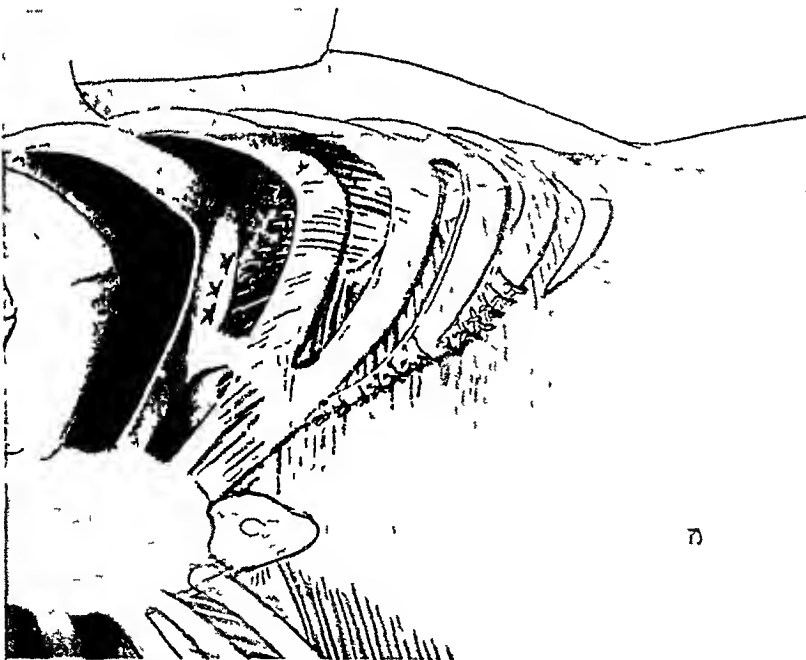


FIG 7—Transverse abdominis sutured to costal arch. Note that common aponeurosis of the transverse abdominis and the diaphragm now lies well above costal arch and that a portion of the transverse abdominis has become a part of the left leaf of the diaphragm

quadrant of the abdomen associated with nausea, vomiting, and fever, duration, about five months. Her mother reported that she had suffered from severe "smothering spells" until she was four and one-half months old.

Examination revealed the presence of a huge right diaphragmatic hernia. Roentgenograms showed no evidence of the right leaf of the diaphragm.

On March 18, 1936, Doctor Brock and one of us (J. D. R.) attempted to close the hernia through an anterior transabdominal approach. When the abdomen was opened, the patient took a deep breath and the entire right lobe of the liver and most of the right half of the colon disappeared into the thoracic cavity. The pleuroperitoneal diaphragm was found to be intact but the fibromuscular septum was represented only by an anterolateral crescentic flap about three inches wide at its widest point (Fig. 8). The posteromedial portion of the diaphragm including the lateral crus was absent. Whether or not the medial crura were missing or merely displaced to the left of the midline was not determined. There were no adhesions. The opening was closed under great tension and recurrence took place in about one and one-half months.

On April 15, 1937, the hernia was repaired successfully by the following procedure. An oblique incision was made over the tenth rib. This rib was excised subperiosteally and the thoraco-abdominal cavity was entered by an incision through the rib bed. It was found that the pleuroperitoneal diaphragm had been ruptured at the time of recurrence of the hernia, and that now the pleural and peritoneal cavities were continuous. Curiously enough, almost no adhesions were found. A careful review of the situation made it clear that the defect in the diaphragm could not be closed without tension, unless some other substance or structure was employed to help bridge the gap. The lower portion of the divided latissimus dorsi seemed to answer this need. Accordingly, it was mobilized, turned in over the eleventh rib, and its free margin sutured to the freely exposed muscle of the posterior margin of the diaphragm by means of "U" sutures of chromicized catgut (Fig. 9). The thoracic cavity was closed by suturing the ninth intercostal bundle and the upper cut margin of the latissimus dorsi to the dorsal surface of the lower portion of the latissimus dorsi (Fig. 10). The result has been quite satisfactory, as can be seen from roentgenograms made three years after operation (Figs. 11 and 12). During this interval the patient has completed a nursing course and is now actively engaged in the practice of her profession.

This procedure was not planned in advance, and we suggest the following improvements: (1) It would probably be better to resect the eleventh rib instead of the tenth. (2) If the latissimus dorsi were divided about two inches above the rib to be resected, a more liberal muscle flap would be provided.

CONCLUSIONS

(1) The diaphragm is continuous with the inner fibromuscular layer of the abdominal wall, that is, the posterior sheath of the rectus muscles, the transversus abdominis muscles, and the anterior layer of the lumbar fascia.

(2) The continuity of the diaphragm with the transversus abdominis makes it possible to use the latter in the repair of large anterior defects in the former. A proposed method of procedure is described and illustrated.

(3) A clinically successful method of repairing large defects in the posterior half of the diaphragm by means of a sliding fibromuscular flap is reported.



FIG 9—Case of Miss B M Defect closed by substituting a part of the latissimus dorsi for the missing portion of the diaphragm

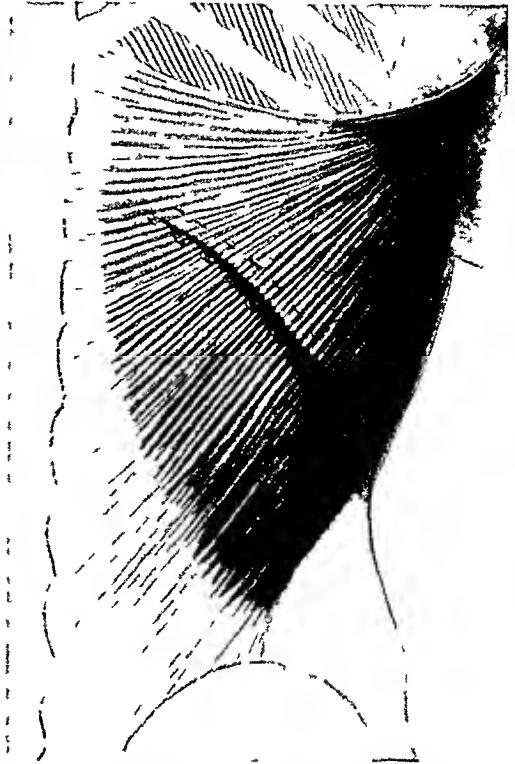


FIG 10—Case of Miss B M Chest cavity closed by suturing ninth intercostal bundle and upper portion of latissimus dorsi to the anterior surface of the lower portion of the latter

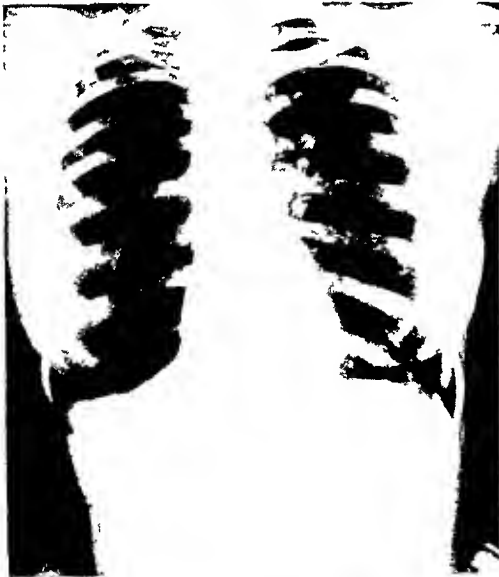


FIG 11—Case of Miss B M Anteroposterior view of chest three years after operation



FIG 12—Case of Miss B M Lateral view of chest three years after operation

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AN OPERATION FOR THE CURE OF INGUINAL HERNIA*

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THE operation which is about to be described is a combination and modification of many of the different technics which have been employed during the last 25 years I have used the same repair, exclusively, in 293 operations during the past five years, and there have been only 2 38 per cent recurrences In 85 per cent of the recurrences, the patients either developed post operative pneumonia associated with a severe cough, or there was a wound infection

TABLE I
SYNOPSIS OF RECURRENCES FOLLOWING 293 HERNIOPLASTIES

No of Cases	Type of Hernia	No of Recurrences	Percentage of Recurrences
171	Indirect inguinal herniae	3	
53	Direct inguinal herniae	2	
32	Indirect inguinal herniae with associate direct hernia	1	
37	Recurrent inguinal hernia	1	
<hr/> Total 293		<hr/> Total 7	2 38%

The incision is the customary oblique inguinal incision The aponeurosis of the external oblique is widely exposed and divided in the center of the superficial inguinal ring (Fig 1) by the aid of a grooved director, care being taken not to injure the ilio-inguinal nerve

The cord is freed, and its fibrous attachments, which are so often found in the region of the pubic bone, are divided (Fig 2), thus allowing the cord to be entirely lifted from the inguinal canal

It is important that the entire inguinal ligament is freed of all adhesions and adipose tissue The superior layer of the aponeurosis of the external oblique is (Fig 3) dissected up to its fusion with the falx inguinalis

The indirect inguinal sac, identified on the anterior surface of the cord, is isolated (Fig 4) and opened, and then dissected free from the cord (Fig 5) This dissection is carried upward as far as possible, so that a portion of the abdominal peritoneum is pulled downward and included in the hernial sac A careful search is made at this time for an associated direct hernia The sac is closed (Fig 6), as high as possible, with No 00 Plastigut,† and after the sac has been cut away, the ligated stump is anchored high under the internal oblique muscle

In the case of a direct hernia, the sac is freed (Fig 7), opened, resected, and closed with a continuous suture of No 00 Plastigut and the operation is completed in the same manner as an indirect hernia

In the case of a large direct hernia, it is often desirable to divide the inferior epigastric vessels, as this will facilitate the exposure and closure of the sac An oblique incision is then carried through the internal oblique muscle

* Read before the Southern Surgical Association, Pinehurst, N C, December 9-11, 1941

† A synthetic product made by the Plastigut Foundation, Peoria, Illinois



Fig 1

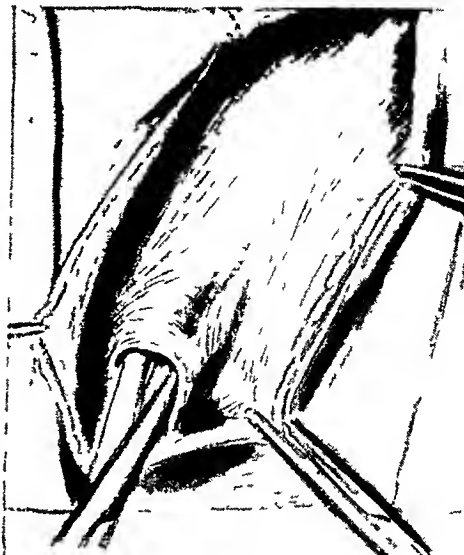


Fig 2

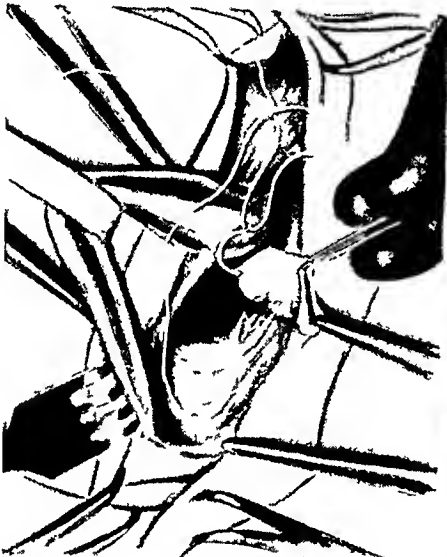


Fig 3

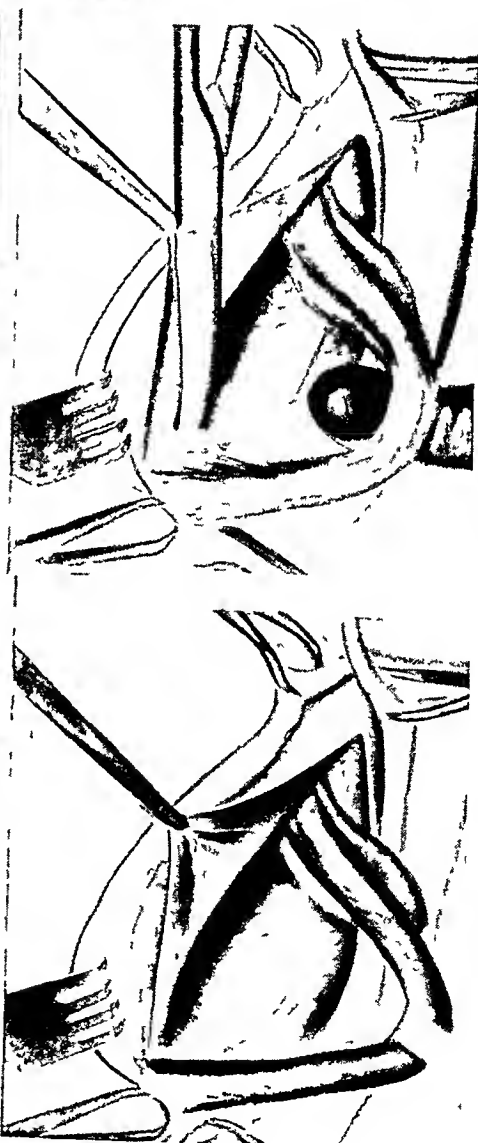


Fig 4

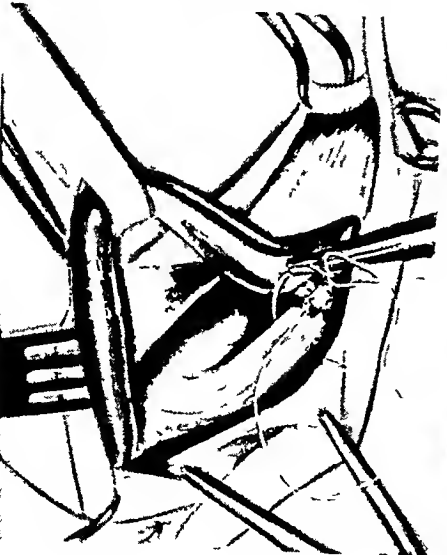


Fig 5

Fig 6



FIG 9



FIG 12



FIG 8



FIG 11



FIG 7



FIG 10

FIG 15

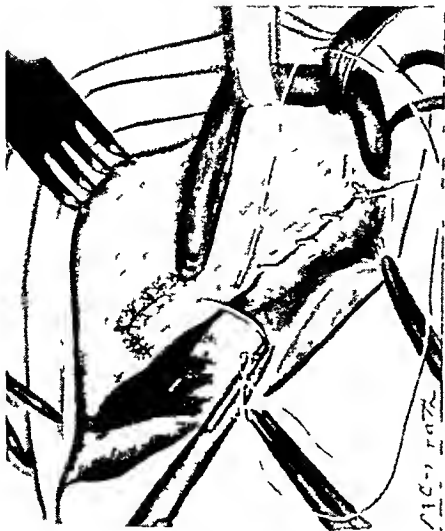


FIG 18



FIG 14



FIG 17

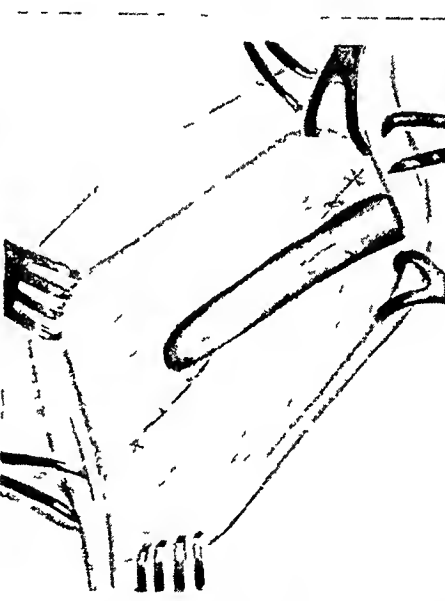
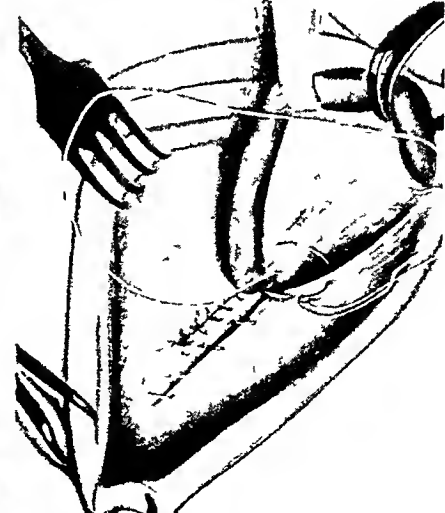


FIG 13



FIG 16



close to the attachment to its aponeurosis (Fig 8), upward and laterally, for a distance of one inch, beginning at the abdominal inguinal ring. The cord is then displaced upward and laterally through this incision, and (Fig 9) the fibers of the internal oblique muscle are sutured around the cord with No 0000 Plastigut, thus forming a new abdominal inguinal ring.

Later during the operation, a flap is cut in the superior reflection of the aponeurosis of the external oblique (Fig 13) and sutured around the cord, thus completing a combined abdominal and superficial inguinal ring. The advantage of this procedure is that there will be no weakness in the subsequent repair, and no strangulation of the cord by too tight sutures, as the cord will not have to be taken into any further consideration in this operation.

The operation is effected with continuous No 00 Plastigut sutures, as this reduces the number of knots and reduces the incidence of serum formation. A small heavy Mayo needle is used. The first suture (Fig 10) is passed through the most medial portion of the falx inguinalis and is carried deeply into the periosteum of the pubic bone, and through the fibers of the inguinal ligament. This suture is tied and a clamp is placed on the free end of the suture. This suture is continued laterally until all of the falx inguinalis and internal oblique muscle (Fig 11) is sutured to the shelving edge of the inguinal ligament. When it has reached the lateral limit of the incision the suture is locked, and a (Fig 12) second row of sutures is placed in the reverse direction, care being taken to place the second row in such a manner that a different level of fibers are grasped in the inguinal ligament. These sutures will have the appearance of cross-stitching. This suture is then continued to the starting point, and tied to the suture which was originally left free.

A flap A B C is cut in the superior reflection of the aponeurosis of the external oblique (Fig 13), one and one-half inches lateral to the cord, so that when it is brought around the cord and sutured (Fig 14) it will complete a new combined abdomino-superficial inguinal ring. The superior reflection of the aponeurosis of the external oblique is now sutured (Fig 15) to the shelving edge of the inguinal ligament, beginning at its most medial attachment. This suture is tied, the free end is clamped, and when the lateral limit of the incision in the aponeurosis is reached, the suture is locked, and is continued medially, imbricating the inferior layer of the aponeurosis of the external oblique over the superior layer, until this same suture reaches its starting point, where it is tied to the suture that was originally left free for this purpose (Fig 16). It will be noted that there are only two knots in the actual repair, but still there are four rows of sutures.

The cord is completely transplanted throughout (Fig 17), lying directly under the superficial fascia and the skin. Scarpa's fascia is closed with a continuous suture of No 0000 Plastigut (Fig 18), care being taken to suture this fascia securely around the cord to the underlying aponeurosis, so as to avoid all dead spaces. The skin is closed with Michael clips, after the wound has been thoroughly cleansed with some aqueous antiseptic or a sterile saline solution.

A METHOD OF DISPOSAL OF THE SAC IN OPERATIONS FOR OBLIQUE INGUINAL HERNIA *

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DURING RECENT YEARS many articles have appeared in surgical literature dealing with the problem of recurrence following operations for inguinal hernia. Many modifications of the original operations of Bassini and Halsted have been devised, all of which have for their object the reducing of the incidence of recurrence. As far as I have been able to observe, most of these improvements in technic have to do with closure of the inguinal canal. I do not wish, in the slightest degree, to minimize the importance of adequate plastic repair of the canal, but I believe that not enough attention is being given to the disposal of the sac.

In 1919, LaRoque¹² described his operation for the removal of the sac from within the abdomen. Later, in 1924¹³ and 1932,¹⁴ he reemphasized the value of this procedure in the various types of herniae. This operation has not gained the popularity it deserves. In 1937, Williams¹⁸ presented a paper in which he discussed the advantages of the abdominal approach to inguinal herniae, as advocated by LaRoque. More recently, Willis,¹⁹ also Harrison,⁹ published papers in which attention was called to the importance of the sac in the cure of hernia. With these exceptions little or no mention has been made of the sac in suggestions for improved technic. Apparently the rôle that the sac plays in the recurrence of a hernia is considered unimportant.

Whatever else may be necessary as a part of the operative procedure for the cure of hernia, the complete removal of the sac from the inguinal canal is essential. The usual practice of ligating the sac as high as possible frequently leaves in the internal ring a process of peritoneum in the form of a cone, with the apex directed toward the canal. This can easily be demonstrated by having a patient, who is being operated upon under local anesthesia, cough or strain, when the bulging peritoneum can be felt by the examining finger. An intraperitoneal dimple is created just proximal to the ligation. This point may well be the beginning of a recurrence.

When the internal ring is unusually large and the neck of the sac is of unusual width, it is technically almost impossible to ligate the sac above the ring. There is an added danger that the ligature may become loosened or even slip off the stump of peritoneum during the postoperative period, because of excessive vomiting or coughing.

If, during an attempt at high dissection, in order to secure a high ligation, the sac, unfortunately, splits up through the ring, or is accidentally buttonholed at or above the ring, the purpose of the high ligation may be defeated. In the description of the technic of hernia operations the importance

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941.

of high ligation is always stressed, but it must be admitted that the so-called high ligation, as generally practiced, is often inadequate. In my opinion, a method of disposal of the sac that will eliminate the dimple or cone-shaped process of peritoneum will contribute, in a large measure, to the prevention of recurrence. If the redundant parietal peritoneum can be tightened over the hernial fossa until it is taut, as suggested by LaRoque, it will certainly constitute the first line of defense against a recurrence of the hernia.

The older surgeons were fully aware of the importance of the complete removal of the sac. Fifty years ago, Bennett⁶ said that the essential requirements of any properly devised operation were "(1) The provision of an effectual barrier across the internal aspects of the aperture through which the hernia escapes, and (2) The abolition of the hernial fossa in the peritoneum over the abdominal orifice of the canal." He further stated that all operations which leave any portion of the sac in the ring or canal are faulty in principle and defective in practice. In my opinion these fundamental principles still hold true.

Before Bassini^{3, 4} made his monumental contribution to the treatment of hernia most surgical authorities considered the complete removal of the sac of primary importance, the canal being regarded as only secondary. As Bassini's methods were not immediately adopted, a number of years elapsed before the older ideas were abandoned. During this period many surgeons devised operations in which the sac alone was the chief consideration. Among them were Macewen,¹⁵ Ball,¹ Phelps,¹⁶ Barker,² Kocher,^{10, 11} Baxter,⁵ Terrillon,¹⁷ and Bishop.⁷ With the general acceptance of the principles of Bassini these operations became obsolete. However, the operation of Kocher, I believe, merits review in detail.

In 1892, Kocher published a paper in which he described his "new" method of operation for the radical cure of inguinal hernia. In this operation, which he called the "transposition-invagination" method, the sac was freed from the cord up to the upper border of the external ring, while strong traction was made on the sac in order to expose its highest part. After reducing its contents, the fundus of the unopened sac was grasped by a narrow, curved dressing forceps and invaginated backward through the inguinal canal, the points of the forceps being kept close behind the anterior wall until they entered the internal ring where they were projected forward through a previously made incision in the abdominal wall well above the level of the internal ring. The fundus of the inverted sac was now forcibly drawn through the opening in the abdominal wall, transfixed, ligated, and excised distal to the ligature. The stump of the sac was then fixed with sutures to the outer surface of the aponeurosis of the external oblique. This disposal of the sac is open to objection, theoretically at least, in that a process of peritoneum is left protruding through the abdominal wall which might conceivably become the site of a ventral hernia. However that may be, his results were excellent, for in this paper he reported 76 cases operated upon with only two recurrences (2.7 per cent), and they occurred in patients who had exceptionally large herniae.

In his "Text Book of Operative Surgery," published some years later, Kocher modified his earlier operation by dropping the stump of the sac back into the abdomen and suturing the opening in the peritoneum and the muscles of the abdominal wall. In those cases where the sac could not be invaginated, either on account of its being too short or too thin, he did what he called

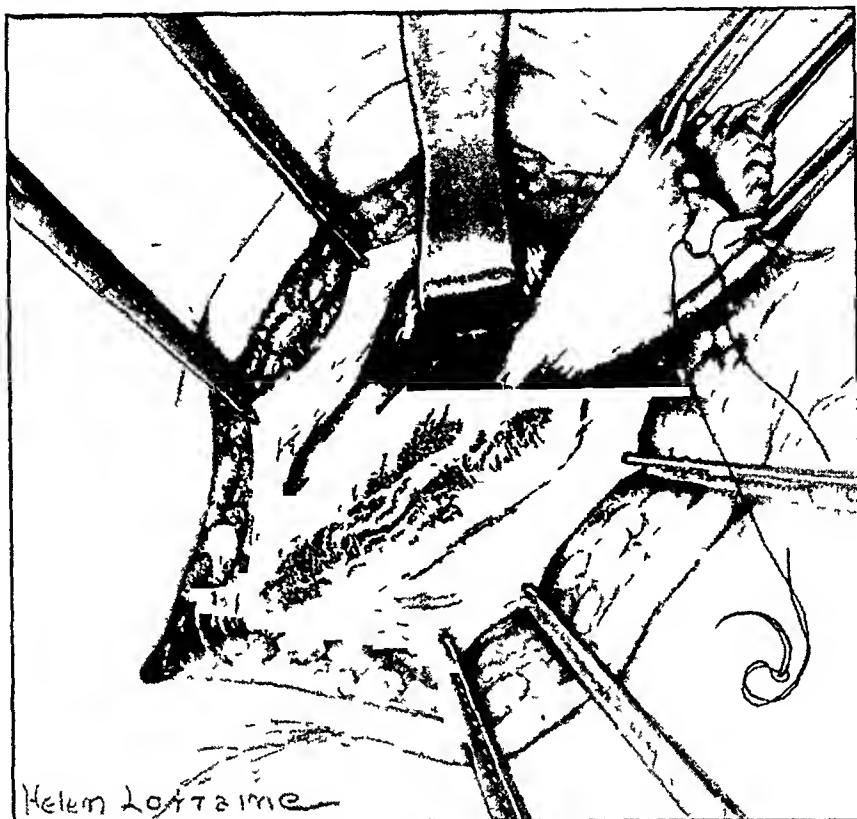


FIG 1—Encircling suture placed in open end of sac, tied loosely with a single knot

"lateral transposition." In this maneuver the sac was grasped with a curved forceps and pushed up the inguinal canal immediately behind the anterior wall as far as the internal ring where it was protruded through a small opening in the aponeurosis and forcibly pulled out. The neck of the sac was ligated, excised distal to the ligature, and the stump allowed to retract into the abdomen. The small opening in the aponeurosis was then sutured.

Kocher was very enthusiastic about his operation, reporting that in his own clinic at Berne, between the years 1896 and 1900, he obtained 97.7 per cent cures—only 2.3 per cent recurrences in 73 cases. He stated further that he considered the cures to be permanent as they had been operated upon over five years. He apparently derived much satisfaction in comparing his results with those of Bassini, who reported, in a similar series of cases, only 90.1 per cent cures, or 9.9 per cent recurrences.

The results obtained by Kocher compare more than favorably with those of the present day. According to Erdman,⁸ "from a number of the largest and best surgical clinics, follow-up reports, based on actual examinations, show from 3 to 7 per cent recurrences after operations for oblique herniae,

and from 15 to 30 per cent after operations for direct herniae. Probably throughout the hospitals of the county the actual rate is even higher."

Kocher's statistics are even more impressive when it is recalled that he did not employ the Bassini method of closing the canal, the treatment of the sac being the principal step in his operation. He simply introduced a series of interrupted sutures beneath the aponeurosis of the external oblique where it forms the anterior wall of the canal, that portion in the grasp of the sutures

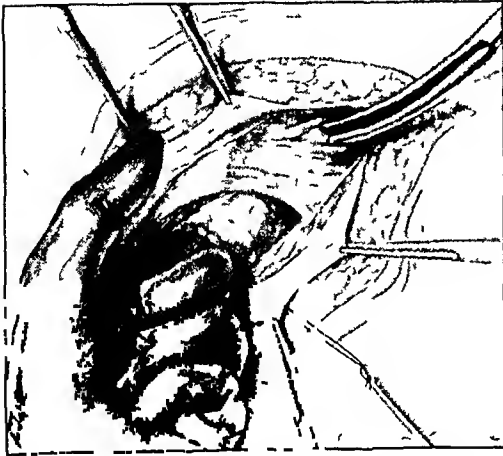


FIG 2—Index finger introduced through neck of sac impinging on anterior abdominal wall the internal oblique and transversalis muscles being separated over tip of finger

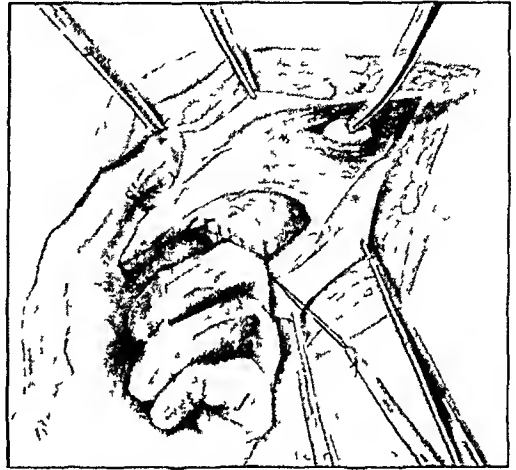


FIG 3—Curved Kelly forceps being used to make puncture opening in transversalis fascia and peritoneum. Forceps is then pushed downward through neck of sac

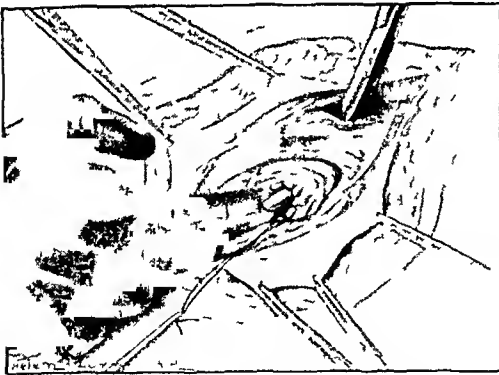


FIG 4—Forceps emerging from mouth of sac in contact with tip of finger

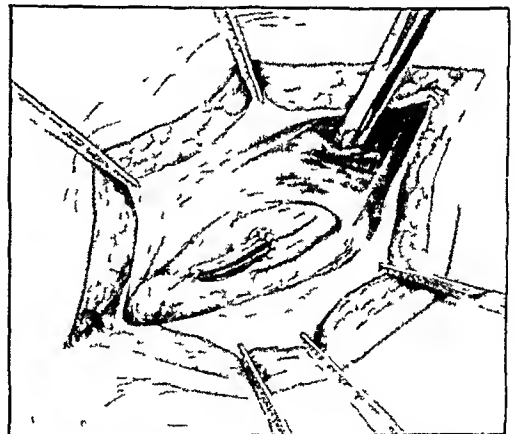


FIG 5—Suture in mouth of sac has been tied around the forceps the ends of suture being engaged in closed forceps

being depressed with the finger so that when the sutures were tied two parallel folds were approximated, thus tightening the aponeurosis and eliminating any redundancy that might be present. The pillars of the external ring were brought together with interrupted sutures closing the ring as tightly over the cord as was possible without interfering with its circulation. He considered Bassini's operation unnecessary in uncomplicated herniae and resorted to it only in instances of strangulation, those complicated by inflammatory thickening of the sac, with visceral adhesions, and in direct herniae

To-day, the fundamental principles of the Bassini operation are universally accepted and practiced, and Kocher's operation has been forgotten. It is probably true that, in the concentration of effort to find better methods of closing the inguinal canal, the importance of adequate removal of the sac has been overlooked. It is logical to conclude that if the modern methods of closure are preceded by a more complete removal of the sac from the canal more permanent cures would result.

For several years I have employed a method of disposing of the sac which, in my opinion, complies with the postulates of Bennett.⁶ It throws an effectual barrier across the internal aspects of the aperture through which the hernia escapes, and also abolishes the hernial fossa in the peritoneum over the abdominal orifice of the canal. It utilizes the principles of Kocher's operation, with important modifications. I must confess, however, that my knowledge of Kocher's operation was acquired during my search of the literature in connection with the preparation of this paper.

TECHNIC OF DISPOSAL OF THE SAC

The inguinal canal having been opened by incising the aponeurosis of the external oblique, the sac is dissected upwards from its bed and freed from its attachments to the cord and cremaster muscle. Any adherent abdominal viscera is released and allowed to drop back into the abdominal cavity. An over-and-over silk suture is passed around the edge of the open end of the sac, completely encircling it, and this suture is tied loosely with a single knot and laid aside (Fig 1). The index finger is then inserted into the open mouth of the sac and passed through its neck into the peritoneal cavity, where it is made to impinge firmly against the anterior abdominal wall at a point two inches above the upper border of the internal ring. The fibers of the internal oblique and transversalis muscles over the impinging finger are then separated down to the transversalis fascia for a distance of an inch or an inch and a half (Fig 2). This separation is held apart by retractors. With a curved Kelly forceps, a puncture is made through the transversalis fascia and peritoneum over the impinging finger (Fig 3), and the point of the blades of the forceps is pushed down through the internal ring, hugging the anterior abdominal wall and in contact with the tip of the finger until it emerges from the mouth of the sac (Fig 4). The suture in the mouth of the sac is drawn tightly around the blades of the Kelly forceps and the knot tied. The Kelly forceps is opened sufficiently to grasp the end of the tied suture and closed (Fig 5). The forceps, grasping the end of the tied suture, is then withdrawn from the punctured opening in the transversalis fascia and peritoneum, drawing the sac through the opening, thereby inverting it. When the sac is thick and bulky the opening may have to be enlarged to permit this procedure. The inverted sac is then pulled outward with sufficient tension to eliminate any redundancy in the parietal peritoneum and thus to abolish the hernial fossa. The sac is transfixed and ligated, the excess distal to the ligature being excised (Fig 6). The stump of the sac is then sutured to the edge of the opening of the transversalis fascia and peritoneum.

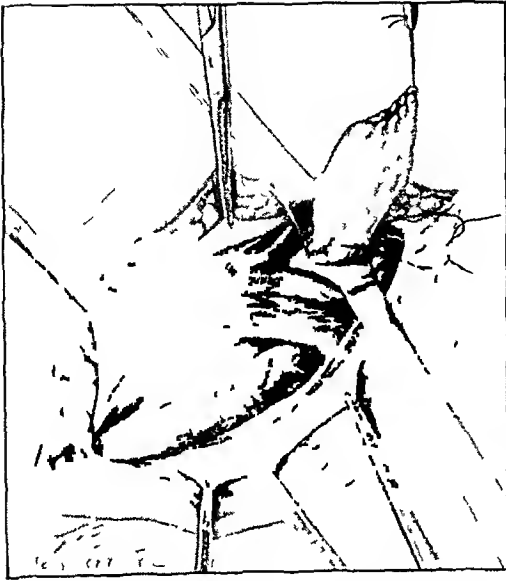


FIG 6—The sac having been inverted through the opening in transversalis fascia and peritoneum, is transfixed and ligated

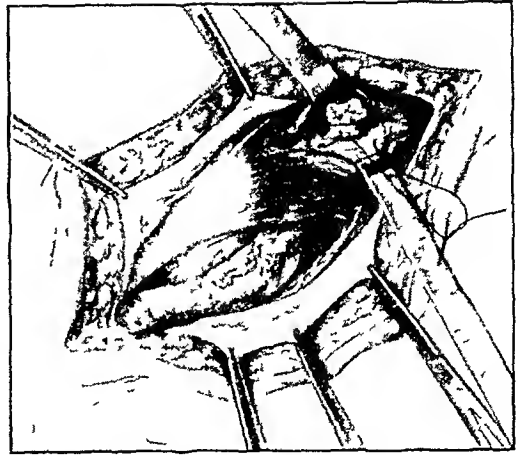


FIG 7—Sac is excised distal to the ligature and the stump is fixed to transversalis fascia and peritoneum with figure of eight suture

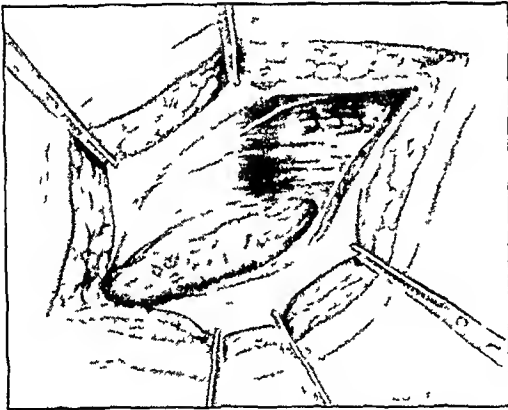


FIG 8—Separation in internal oblique over transversalis muscles is closed with several interrupted sutures

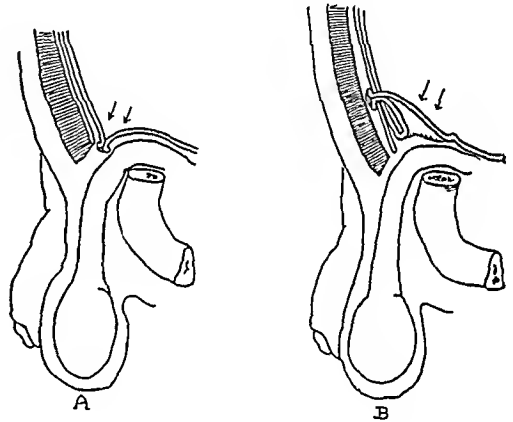


FIG 9—Diagrammatic representation of the appearance of a cross section of the region at the internal abdominal ring (A) When sac is ligated high in ring (B) When sac is inverted

with a figure-of-eight suture (Fig 7) The opening in the oblique and transversalis muscles is closed with several interrupted sutures (Fig 8) The inguinal canal is then repaired according to the desires of the surgeon

CONCLUSIONS

This method of disposal removes the sac from the inguinal canal and places a barrier over the internal aspects of the internal ring. This can readily be demonstrated by passing the finger into the resulting peritoneal covered cone where the tense peritoneum can be felt holding the abdominal viscera well away from the inguinal region. It is simple of execution and adds perhaps five minutes to the operating time. It is not offered as a substitute for the Bassini technic, notwithstanding Kocher's results, but as a more effectual method of disposing of the sac. If employed in conjunction

with the modern methods of closing the inguinal canal, the rate of recurrence should be decreased

This procedure has been employed in 66 cases, followed by the Bassini closure of the canal. To date, there have been no known recurrences. Many of these cases have been operated upon within recent months, and it is not possible, as yet, to evaluate the effects of this method of disposal of the sac, on the percentage of recurrence.

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DISCUSSION —DR CHARLES R. ROBINS (Richmond, Va.) It will always be difficult to bring out anything new. With reference to the illustration shown by Doctor Mastin, with the incision across the fibers of the internal oblique muscle, I found the same incision in a book by Bloodgood that I ob-

tained from a sale of Dr Howard A Kelly's library, which gave a résumé of all operations for hernia performed at Johns Hopkins Hospital up to 1894.

I am quite confident that the question of recurrent hernia will be settled in the Southern Surgical Association. We had a paper by Doctor Estes last year, in which he reported a low percentage of recurrences, and another member, Dr Thomas M Joyce, of Portland, Ore., published a remarkable series in the Journal of the American Medical Association.

I think some of the trouble we have in recurrent herniae is due to the incision. The real defect is over the pubic bone, and no incision is complete that does not expose the region of the pubic bone and the insertion of the rectus muscle. Doctor Mastin has been very fortunate in his cases because all his illustrations show a very fine conjoined tendon. One reason for recurrences is that there is no conjoined tendon. If you investigate your cases of inguinal hernia you will find this muscle to be deficient in direct hernia and very often in the indirect type.

The most important maneuver is to place the patient in the recumbent position and at ease. The finger is placed on the scrotum at a point which will permit its invagination. The finger is then passed along the cord up to the external ring. If the finger then can enter the abdomen in contact with the superior and posterior surface of the pubic bone the conjoined tendon is either absent or very poorly developed. Otherwise the finger could not enter the abdomen.

I would like to say that my approach to the hernia question, and my reason for discussing it at this time, is based on the fact that I am preparing a series of operations in which I have performed either the third or fourth operation for that particular hernia. This shows that whoever operated upon these cases before—the best surgeons in my section of the county—have left some hole that is not stopped up, and everyone knows that in direct hernia recurrences appear promptly.

The speaker here showed a series of slides illustrating the following conditions:

The first slide (Cunningham's Manual of Practical Anatomy) shows a normally developed conjoined tendon. It originates from the outer segment of Poupart's ligament and passes over the cord, and is inserted behind the cord in the iliopectineal line and the crest of the pubes. This contracts on the cord when there is increase in intra-abdominal pressure, as in coughing, straining, *etc.*, and produces the shutter action described by Sir Arthur Keith. It probably has a very important function in obliterating the processus vaginalis, the process of peritoneum which precedes the descent of the testicle.

The next slide shows the deficiency of the lower segment of the internal flat muscles, including absence of the conjoined tendon. The fibers pass directly over to the sheath of the rectus. In such a case a well developed sac of indirect hernia is often found in addition to the direct hernia.

A series of slides show a recurrent hernia with the sac of a direct hernia and also a femoral hernia. After the bifurcated sac (direct and femoral hernia) was removed, the finger could be introduced under Poupart's ligament through the femoral ring. The repair was effected by the fascial suture derived from the median pillar of the ring which attached the rectus muscle and sheath and the lower segment of the internal flat muscle, to the crest of the pubes, Gimbernat's ligament and Poupart's ligament. This effectively closed the muscular defect and also the femoral ring.

The last slide shows a young man, age 23, in whom there was muscle deficiency on both sides, a developed direct hernia on the left side, together with a well formed sac of indirect hernia, and on the right side a small

peritoneal sac projecting in the upper part of the cord together with the muscle deficiency, but with no protruding sac of either direct or indirect hernia. This case shows that the muscle deficiency is a congenital condition.

DR WILLIAM F. REINHOF (Baltimore, Md.) It has been indeed a pleasure to hear these three papers, as well as Doctor Robins' discussion. I wish to comment on the statement made by Doctor Mastin, that most of the recurrences in his series of cases operated upon for the cure of inguinal hernia have occurred at the upper angle of the wound. This is contrary to my experience and that of other members of the staff of Johns Hopkins Hospital. Apparently most recurrences in our cases have developed at the lower angle of the hernial wound. It is quite true that in Baltimore, as elsewhere, various technical procedures are employed. The obvious lack of unanimity of opinion in regard to operative treatment is based on the fact that in a certain number of patients, although this is a small percentage, the operation has failed to bring about a cure.

A most cursory review of the literature will reveal that each year articles on the operative treatment of this condition have been published, indicating that in spite of the fact that the majority of cases are now easily and permanently cured by a variety of procedures by the average operator, there is, nevertheless, a small but definite group in which recurrence is all too common.

It has been called to my attention, after dissection of more than 300 bodies during the course in surgical anatomy, in the last ten years, how infrequently one can demonstrate tendons which are described as normally occupying the lower inguinal region. For instance, in the cadaver in which no hernia exists, it is quite unusual to be able to demonstrate a conjoint tendon, and by conjoint tendon I mean the fusion of the transversus and internal oblique fascia lateral to the attachment of this fascia to the lateral edge of the rectus sheath. It is almost never possible to demonstrate a conjoint tendon due to fusion of the transverse and internal oblique aponeurosis as far lateral as the internal inguinal ring. It is more frequent, in the dissecting and operating rooms, to find the internal oblique muscle and its aponeurosis the more strongly developed of the two, and inserted separately on the ventral sheath of the rectus muscle. The falx inguinalis, in the absence of the conjoint tendon, is usually contributed to mainly by the aponeurosis of the internal oblique. The weakness or strength of the lower inguinal region is, therefore, in direct proportion to the strength of the aponeurosis of the internal oblique and transversus muscles between the internal inguinal ring and the lateral edge of the rectus sheath. If they are fused, the structure should be termed the conjoint tendon, which may be strong or attenuated in young or old, in the presence of or absence of hernia.

If the aponeurosis of the internal oblique and transversus muscles are not fused, the conjoint tendon is absent, but the sickle-shaped band of fibers in the accentuated aponeurosis of the internal oblique muscle, the falx inguinalis, may be, and usually is, present and definable. In adult cadavers and operative cases examined, the aponeurosis of the internal oblique and transversus muscles together, in the great majority of instances, have been found to be atrophic, indefinite and attenuated, rather than definite, strong and readily demonstrable. Thus, unless some technical method is devised to overcome this absence of fascia at the lower angle of the wound, the closure is bound to be insecure. This insecurity may be due to a paucity of tissue, as a result of which there is tension on the suture line which approximates the attenuated fascia of the transversus and internal oblique muscles to Poupart's ligament.

For these reasons, I wish to call attention to a simple procedure which not

only augments the fascia present in the lower inguinal region, but at the same time permits secure closure without producing the slightest tension, and thus remains true to one of the greatest and most fundamental surgical principles. This consists of a vertical incision made over the anterior sheath of the rectus and pyramidalis muscles down to their insertion in the pubic bone. The incision in the rectus sheath is carried down to the superior ramus of the pubic bone, and, superiorly, it may be continued as far as the reflection of the aponeurosis of the external oblique will permit. This incision releases the anterior rectus, and the enclosed muscle tends to bulge immediately. Lateral displacement of the rectus sheath is then accomplished easily, and the closure of the hernial wound is carried out in close accordance with the technic described by Halsted. This procedure is to be distinguished from the one originally suggested by Doctor Halsted, namely, turning over the flap of the rectus fascia as a door on a hinge, and suturing the cut end to Poupart's ligament, it will be noted in that procedure that there is a weak area at the lateral border of the rectus muscle. In the method I propose, the sheath is simply displaced and drawn laterally, so that the lateral edge of the muscle is not exposed and in time the anterior sheath grows back over the surface of the rectus muscle. In this way tension is avoided without the use of fascial strips. This procedure is to be especially recommended in operations for bilateral herniae.

DR BRADLEY L COLEY (New York, N Y) I should like to discuss the last three papers in a general way, without specific reference to any one of them. I believe we are all convinced that recurrences after hernia operations may be due to many factors, some of which are perhaps within our control, but many of which are not. Among the latter may be mentioned the surgical anatomy of the individual and the character of the tissues comprising the region through which the hernia escapes. Indirect inguinal hernia tends to recur either within the internal ring or at the lower angle just above the pubic bone. Recurrences at the internal ring may be due sometimes to an unnoticed indirect sac or an inadequately high ligation and excision. It is to prevent these recurrences that methods of disposal of the indirect sac, such as that described by Doctor Collins, have been devised.

Personally, I agree with Doctor Reinhoff that the majority of recurrences take place at the lower end of the canal. The reason here lies in a defect in the transversalis fascia and the high insertion of the internal oblique and transversus abdominis muscles to Poupart's ligament. To provide a bulwark for this undefended area (Hesselbach's triangle) is the aim of most operations for direct hernia, and it is to strengthen this area in particular, that Doctor Robins has worked out his operation. I believe that the rôle of the transversus muscle in effecting a firm repair in direct hernia has not been fully appreciated. The transversalis fascia is invariably thin and attenuated in cases of pronounced direct hernia. The transversus aponeurosis, however, is usually a fairly firm layer, and this can be sutured to Poupart's ligament as the first or deepest layer of the repair.

In the present crisis which confronts us, large numbers of men will be examined with a view to determining their fitness for serving with our armed forces. Many of these Selectees will be rejected because of so-called *potential hernia* or because of large inguinal rings. Those rejected will, as advised, seek operation for a cure of the so-called hernia. I can recall just after the First World War, while working under Dr William A Downes, that we encountered a goodly number of recurrent inguinal herniae in soldiers who had undergone operation for alleged herniae which had given them no symp-

toms and which were, in reality, large inguinal rings, or so-called impulses. These direct recurrences were often difficult to cure by further surgery, a number of them had successive recurrences and were never relieved. Therefore, I should like to make a plea for a more positive evidence of hernia before subjecting these borderline cases to operation.

DR CHARLES GREEN (Houston, Texas) I think there are two important points in the repair of hernia. First, choice of anesthetic, and second, prevention of tension on the soft parts.

Several years ago I reported 315 cases of herniae before the Railway Section of the Southern Medical Association, with less than 2 per cent recurrences. I feel that this low percentage of recurrences was due, first, to the fact that the majority of the operations were performed under spinal anesthesia, thus avoiding the stage of excitement following operation, when the patient is reacting from a general anesthetic. I have seen patients waking up from a general anesthetic become so excited that it took two or three orderlies and nurses to keep them in bed, and only the Lord himself could keep them from tearing the repair of the hernia before regaining consciousness. This does not occur when spinal anesthesia is used. Local anesthesia is good, but because of the multiple punctures into the soft parts to produce local anesthesia there is more danger of postoperative infection than when spinal anesthesia is used. The second point is that we were very careful to see that no great amount of tension was produced when the hernia was repaired.

Personally, I do not feel that the best results can be accomplished in hernia repair without transplantation of the cord. In my hands the Bassini method of repair, with my modification of Bloodgood's modification and transplantation of the cord, is the best technic.

In closing, let me state that I cannot agree with Doctor Collins that the most frequent site of recurrence is the internal ring. My experience has been that recurrences are in the form of a direct hernia just over the pubic bone, at the most fixed point. However, Doctor Collins' technic certainly does away with any weakness at the internal ring.

DR R. DUVAL JONES (Norfolk, Va.) In 1934, my associate, Dr. R. L. Payne, published, in the November issue of the Southern Medical Journal, a report of his results in the repair of 200 consecutive cases of inguinal hernia. With this report he published illustrations of a standardized technic which he had employed, using a strip of living fascia from the inner leaf of the external oblique aponeurosis for his main suture. His report was most gratifying and, since that time, we have built up our series to approximately 500 cases with continuous good results. We have had three known recurrences. The first recurrence was a direct result of the patient's falling down stairs while intoxicated, only three weeks after operation. The second, we attribute to a failure to close the defect sufficiently snug at its lower angle, and the third occurred in an elderly fat man as a result of infection around interrupted silk sutures which were used to reinforce the fascial suture.

I agree with Doctor Reinhoff and Doctor Robins that the two most common sites of recurrence are (1) where the neck of the sac opens into the peritoneum, and (2) the lower angle of the triangular space where it is often difficult to completely obliterate the defect. However, I am convinced that these weak points are satisfactorily overcome in the great majority of cases by carefully carrying out the technic which Doctor Payne and I have used in our series. This is simply a modification of Bassini's operation, utilizing a strip of living fascia from the inner leaf of the external oblique aponeurosis for the main suture.

The salient points in carrying out Doctor Payne's technic were here shown by the speaker by presenting several slides

Slide I shows the point of the index finger in the external ring and the method of cutting out the fascial suture from the inner leaf of the external oblique aponeurosis which is left attached to the pubic bone

Slide II shows the method of closing the neck of the sac at its highest point on a level with the parietal peritoneum after the sac has been dissected free and the contents have been reduced

Slide III shows the fascial suture threaded on a large fascial needle and fixed with a single catgut tie. The suture is then placed under the cord and is used to approximate the conjoined tendon to Cooper's and Poupart's ligaments, thus closing the defect and providing a new bed for the cord. It is in the placing of the first stitch of this suture that one should be most careful to include Cooper's ligament, lest there be left a small opening through which recurrence may occur

Slide IV shows the defect closed, a new floor having been made for the cord by suturing the conjoined tendon and arching fibers of the internal oblique to Poupart's and Cooper's ligaments, and fixation of the fascial suture with interrupted chromic catgut or silk sutures. Insert A shows the free end of the fascial strip being split, B shows the method of fixing the split ends with a square knot, and C shows the method of turning down the split ends after the square knot has been tied, and fixing them with chromic catgut or silk

It has been a great privilege to hear these excellent papers and discussions on hernia, and I offer my discussion simply because I feel that, at least in the hands of Doctor Payne and myself, the technic I have attempted to describe has continued to give sufficiently good results to justify calling it to your attention

DR AMOS KOONTZ (Baltimore Md) I am sorry to prolong this discussion, but I would like to refer to what Doctor Coley has said about operating upon cases which have simply an enlarged ring. Fortunately, the Army regulations are definite on this point, and state that a diagnosis of hernia shall not be made on the basis of an enlarged ring and slight impulse alone. The diagnosis is to be made only if a sac is demonstrable. In the early days of selective service examinations some of our best surgeons turned down men who should not have been rejected. These doctors were working as civilian employees at army examination stations and we had a tough time educating them to the point where they did not reject men improperly. Many men with enlarged rings and slight impulses go through their whole lives with this condition and never develop a hernia. I agree with Doctor Coley that operating upon such cases, especially under war conditions, may make hernia cases out of some of them

With reference to Doctor Cannaday's paper on cutis graft, although I have had no experience with such grafts there is evidence for believing that what he says about the ultimate fate of the graft is correct. In experimental work which I did some years ago, I showed that when a piece of the rectus sheath is removed it regenerates in a very short time, and very often the regenerated sheath is stronger than the original fascia. In the case of the cutis graft, I expect that the ingrowth of fibrous tissue from the surrounding rectus sheath eventually makes the graft stronger than it was at the time of implantation. It seems to me however that there are two objections to the operation. The first is the removal of a large piece of skin from some other part of the patient's anatomy. In the second place, one would think that the flimsy nature of the cutis graft would make it unsuitable to resist

the impact of the intra-abdominal pressure. In these cases I am still using large sheets of preserved ox fascia, as described in the Archives of Surgery, in March, 1933. In using preserved fascia there is one thing that must be remembered. It is preserved in a chemical solution which is irritating to the tissues and, therefore, the fascia should be thoroughly washed in salt solution prior to its use. At one time the firm that puts out ox fascia changed the preserving solution, and started to put it up in a very irritating solution which caused sterile abscesses. This caused the material to get a very bad name, which it certainly deserved as put up in that particular preserving fluid. However, as soon as this was brought to my attention the obnoxious fluid was quickly eliminated and the material is now put up in a solution of 1 per cent bimodide of mercury in alcohol. The present material is very satisfactory and is used with excellent results by a great many surgeons. Doctor Stone recently told me that in his operation for anal incontinence he can see no difference in the results between preserved ox fascia and autogenous fascia. Dr. Henry Cave of New York has the fascia soaked in salt solution for two hours before using it. It is my practice to have the nurse, as soon as she is scrubbed up, break the tubes of fascia, thoroughly wash them in salt solution and then put them in a second basin of salt solution to soak until they are used.

I was much interested in Doctor Collins' method of dealing with the hernia sac, and believe that his method presents a simplified procedure for carrying out LaRoque's principle.

With regard to Doctor Mastin's paper, I thoroughly subscribe to the principle of subcutaneous transplantation of the cord, which was the essential part of the original Halsted operation. There seems to be a definite trend back to this procedure. It seems to me to have two distinct advantages. In the first place, it allows very tight closure of the lower end of the suture line, which is the point at which most herniae recur. In the second place, the subcutaneous transplantation has the advantage over transplanting it between any of the other layers, in that it allows the muscle and the two layers of the imbricated aponeurosis of the external oblique to grow together in a solid sheath which, it seems to me, presents a much stronger bulwark against intra-abdominal pressure than if any of these layers are separated by having the cord between them.

DR JOHN E. CANNADAY (Charleston, W. Va., closing). With reference to the subject of inguinal hernia, our results have been considerably improved since we began using single, interrupted cotton thread sutures. In regard to the use of the cutis graft, for certain large herniae, which used to be considered inoperable, it is by far the most satisfactory method I know of.

DR JOSEPH D. COLLINS (Portsmouth, Va., closing). The procedure I have suggested does not entirely solve the recurrence problem. However, I believe it will serve as a first line of defense against recurrence. It is particularly applicable where the neck of the sac is of such width that it is impossible to ligate it above the internal ring.

As Doctor Green has stated, when a patient reacts from a general anesthetic in a state of delirium there is always a danger that the plastic repair of the canal may be damaged. This damage may be the inception of a recurrence. By using this method of disposal of the sac, the abdominal viscera will be held away from the suture line until firm union between the conjoined tendon and Poupart's ligament has taken place.

DR E. V. MASTIN (St. Louis, Mo., closing). I feel sure that Doctor Robins must have misunderstood me, as I did not intend to give the im-

pression that recurrences do not occur at the lower end of the wound, for I am certain that the greater number of recurrences do occur there. So much attention has been paid to this fact that many surgeons have adopted a technic of transplanting the cord directly under the superficial fascia, thereby completely closing the lower angle with the falx inguinalis and two layers of the aponeurosis of the external oblique muscles, thus making such a strong closure that recurrences seldom occur at this point. With the lower angle taken care of, the other point of weakness I have encountered has been around the cord, and the technic I have described has minimized this. Formerly I had some difficulty with swelling of the testicle due to trying to close the fascia around the cord too tightly, but since cutting the internal oblique muscle and changing the position of the cord, I have had no difficulty with this swelling, and have not found it necessary to use a scrotal support for more than a year. In cases where the falx inguinalis was not sufficiently strong to give adequate protection at the medial angle of the incision, I have made a practice of cutting a portion of the rectus sheath and bringing it down with the falx inguinalis to strengthen this defect, but this has only been necessary in a relatively small number of cases.

THE USE OF THE CUTIS GRAFT IN THE REPAIR OF CERTAIN TYPES OF INCISIONAL HERNIAE AND OTHER CONDITIONS*

JOHN E. CANNADAY, M D

CHARLESTON, W VA

BY THE TERM "cutis graft" or "dermal graft" as used in this paper, is meant an excised area of skin, usually with an underlying layer of fat, from which the epidermal layer has been removed and which has been implanted into the body tissues. Otto Loewe,¹ of St Marks Hospital, Frankfurt-on-Main, apparently first made use of the cutis graft. In 1913, he reported his results in nine cases. In 1929, he reported on his use of cutis grafts in about 100 patients, including all types of cases in which fascia had hitherto been used, including such operations as replacement of damaged dura, repair of large incisional herniae, fractures of the long bones, arthroplasties of the knee, hip and elbow joints, and habitual dislocation of the shoulder joint, he employed cutis material in the form of sutures and ligatures, also for suspension or fixation with generally good results.² He observed that these grafts heal in place and become firmly attached even under unfavorable conditions.

Rehn³ published his first report of cases in 1914. Later in his monograph on the use of cutis transplants he described two reconstruction operations performed by him in the fall of 1913, in which destroyed portions of hand tendons were replaced with strips of cutis. He began using cutis grafts in connection with various reconstructive operations in which fascia had hitherto been used. Rehn⁴ believed that cutis was the most suitable material for repairing certain defects because it best answered the requirements for tissue regeneration as outlined by Roux.⁵ He believed that the tension under which the graft had been sewn in place acted as a stimulus to the bringing about of a gradual metaplasia of the transplant.

Uihlem,⁶ who checked over a total number of 104 case records of patients operated upon by Rehn since 1928, in the University Clinic at Freiburg, noted 15 wound infections, of these the results in nine were good, six not satisfactory. Four patients died from pneumonia. Of the total number there were 65 incisional herniae, 11 inguinal herniae, eight knee joints with lateral motion, 20 miscellaneous. The late results in 70 were good, in 14 poor, results unknown, 20 cases.

Eitner,⁷ during World War I, made extensive use of transplants of skin, fat and fascia, separately or in combinations, as free or attached transplantations in the course of plastic operations. He reported on this work in 1920, and stated that the results with the use of derma were more permanent than when other material was used.

The subject of cutis grafting has been discussed in some detail by Maingot,⁸ also by Fomon,⁹ Davis,¹⁰ Byars,¹¹ and his associates, likewise Barnes,¹² Straatsma,¹³ Smith,¹⁴ and Peer,¹⁵ all have made use of dermal grafts for filling out defects, particularly in the region of the face and head, and have

* Read before the Southern Surgical Association, Pinchurst, N C, December 9, 1941

found them satisfactory. In this type of surgery at times more than one thickness of dermal tissue is used.

Experimental Work—Rehn,¹⁶ and Schwartz,¹⁷ in operations upon dogs, removed a portion of the Achilles tendon and closed the defect with a cutis graft. In ten weeks the repaired tendon, functionally and structurally, closely resembled the control tendon on the opposite side.

Eitel,¹⁸ by means of Warburg's method for estimating tissue metabolism, showed that the metabolic rate of derma was considerably higher than that of



FIG. 1—Hernia prior to operation, anterior view

fascia. Work done by Davis and Tiaut,¹⁹ Carnot and Deflandre,²⁰ and Barker,²¹ in regard to burying full-thickness skin, showed the feasibility of securing satisfactory "takes" after practically all such implantations. Peet and Paddock²² had histologic sections of human derma made at intervals of from a week or ten days up to a year or longer after implantation. They found, in most instances at least, that even though a careful attempt was made to remove all the epidermis from the graft prior to its implantation, some epidermal tissue was left, that the sebaceous glands and hair follicles disappear early, that the sweat glands disappear later and undergo gradual transformation into fibrous tissue, that the derma survives by fusion with the adjacent subcutaneous tissue, and that this is brought about by the mechanism of inflammation and repair associated with aseptic wound healing.

Advantages—Cutis is better suited for plastic repair than fascia because it is more active and has longer life. It makes a repair that is stronger and more resistant to the impact of pressure or strain. Cutis is more readily available. According to the laws of the mechanism of development derma could be expected to undergo a type of transformation according to its use. Cutis takes readily and heals in place firmly in a comparatively short time.

Operative Technique—The operative procedure is essentially the same as that used for the implantation of fascia. After making as thorough a closure of the hernial opening as possible by the usual surgical methods, the epithelium is removed from a suitable area of skin, preferably situated on the antero-external aspect of the upper third of the thigh. However, cutis from the skin covering the hernia or other areas will be found almost as satisfactory. This cutis is cut into a suitable shape so as to overlap moderately the fascial edges surrounding the hernial opening. A thin layer of fat, usually about

2.5 mm in thickness, is left underneath the graft. The graft is placed and sutured under firm tension with Nos. 30 or 40 (usually the latter) interrupted cotton thread sutures spaced at frequent intervals. By the use of a double graft, that is, by suturing one graft either to the peritoneum and posterior fascia or to the undersurface of the aponeurosis and the other on top of the aponeurosis, we ensure a much stronger abdominal wall. Sulfanilamide crystals and sulfathiazole in small amounts (usually not more than 2 Gm. of each) are placed between the different layers of tissue. The subcutaneous tissue is

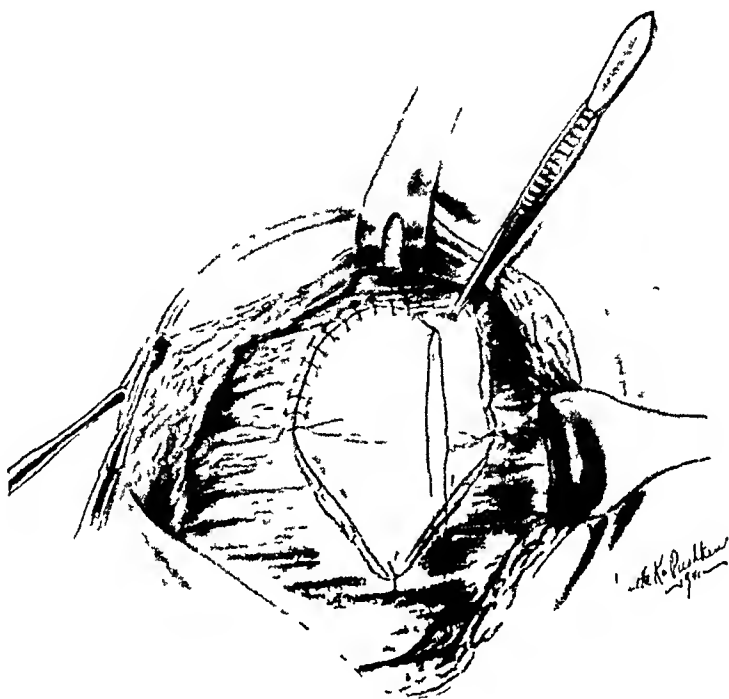


FIG. 2—Cutis graft being sutured to rectus aponeurosis

sutured over the graft with cotton thread sutures Nos. 60 or 70. No tension sutures are used in the wound closure. Skin clips are used in closing the skin edges, and No. 70 cotton thread sutures are placed between the clips, each suture taking a very small bite of skin.

It has been advised by Rehn,²³ and some other German surgeons, that hernia cases in which cutis implants have been used, be kept in bed from six to ten weeks with a view to waiting until the transplant had been to a considerable extent converted into fibrous tissue. My observations lead me to believe that the skin implant is very firmly united as early as three weeks subsequent to implantation, and that prolonged rest in bed is not necessary.

In the formation of replacements for damaged tendon the cutis tissue may be used either in a single strip or strips braided or twisted together, in the replacement of large tendons such as the tendo achillis, a flat strip of skin with the edges sutured together as a tube with the fat side out.

The indications for the use of cutis are essentially the same as those for

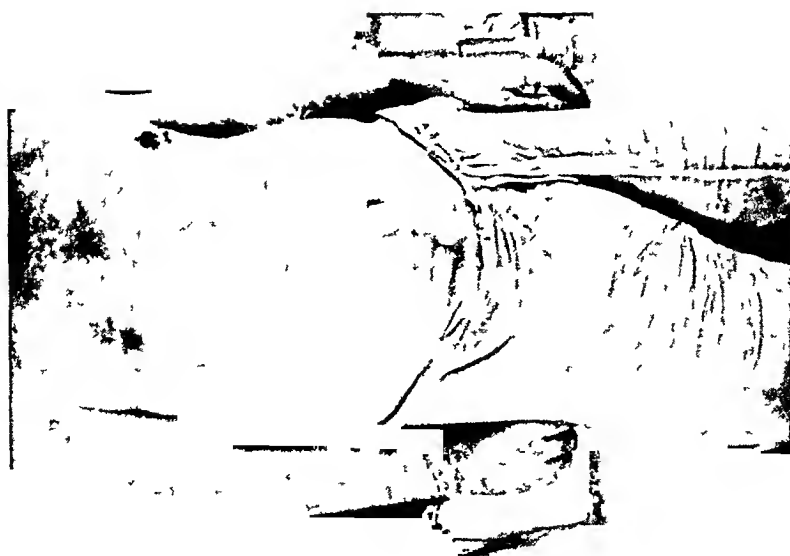


FIG 3—Hernia ten weeks after operation

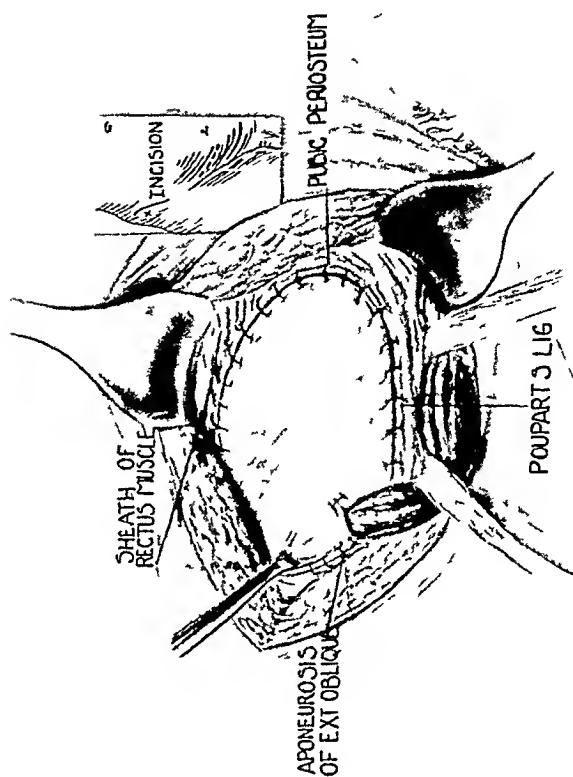


FIG 4—Cutis graft repair of large direct inguinal hernia

the use of fascia or tendon, cases of large incisional herniae in which the edges of the aponeurosis cannot be made to overlap, inguinal herniae in which the structures surrounding the opening are defective or those in which the structures about the ring cannot be approximated without undue tension, tissue replacement after excision of the patella, the reconstruction of unstable knee and elbow joints by using grafts to replace or to supplement weak or absent external ligaments, habitual dislocation of the shoulder, also lower jaw, the filling out of depressions due to the loss or absence of tissue, the replacement of portions of tendon that have been destroyed, the use of strips of cutis for suture material, suturing the ends of fractured bones together, securing bone grafts in place, the anchoring of either end of the dislocated clavicle, arthroplasties of elbow, knee and hip joints

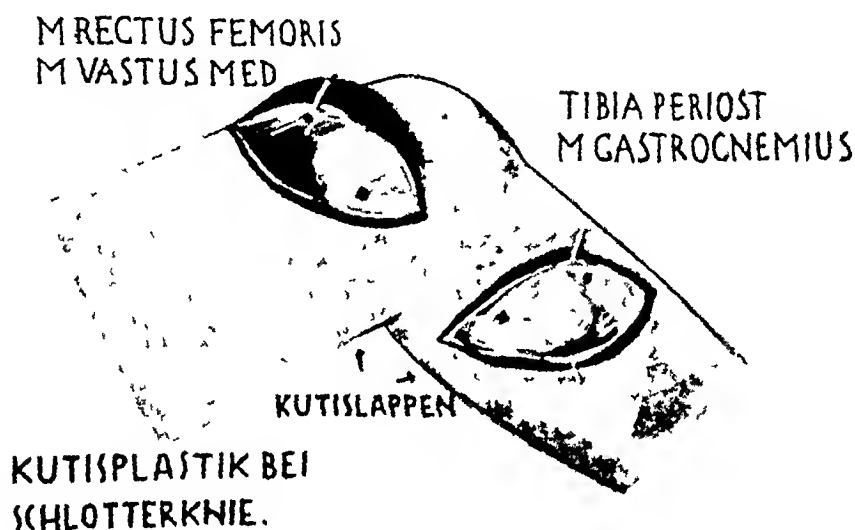


FIG 5—Cutis graft in place showing incisions for insertion in case of slipping knee. Translation (German terms) *Kutislappen*—Skin flap. *Kutisplastik bei*—Cutis plastic for *Schlotterknie*—Side slipping or wobbling knee. (After Rehn Arch of Surg, 38, No 1, 127, January, 1939. Article by Alfred Uihlein, Jr.)

We have used cutis grafts in the repair of six large incisional hernias (in one of these a double thickness graft was used), five large indirect inguinal hernias with defective structures (two of these by Dr Bankhead Banks, one by Dr Hugh A. Bailey, both surgical associates), one repair of double fracture of the patella, one on-lay bone graft for ununited fracture of ulna, one suspension of the uterus, all with primary healing and apparently satisfactory results

ILLUSTRATIVE CASE REPORTS

Case 1—B. P., white, male, age 51, admitted to the hospital May 27, 1940 with a very large epigastric hernia. The bulge on deep expiration was fully $4\frac{1}{2}$ inches across. He had a small ulcerated area over the hernia. A wire screen was placed over this and the patient was kept in the hospital for 3 weeks at the end of which time healing had taken place.

Operation—July 9. The hernial sac was excised, parietal peritoneum was closed by overlapping. The edges of the muscular aponeurosis could not be approximated. A cutis graft from the thigh was sutured over the defect. The patient had an uneventful con-

valescence A recent check shows no evidence of recurrence He returned to his former occupation of coal loading several months ago

Case 2—T L K, white, male, age 69, admitted to the hospital April 19, 1941 for repair of a large lower right incisional abdominal hernia Weight 170 pounds Blood pressure 170 systolic, 110 diastolic The size of the hernial bulge was approximately that of an average baby's head

Operation—May 8, 1941 The hernial sac contained several loops of small bowel The opening in the aponeurosis was approximately 4 x 2 inches wide This was closed by use of a cutis graft from patient's thigh He made a satisfactory recovery with no evidence of recurrence to date

Case 3—H T, white, male, age 23, was admitted to the hospital, December 21, 1941, with two transverse fractures of the patella, and a nearly complete transverse laceration of the patellar aponeuroses, also, a considerable laceration of the skin over the patella

Operation—January 5, 1942 Open reduction of the fracture was effected, together with repair of the aponeuroses over the patella by a cutis graft-suture taken from the skin of the thigh just above the knee This was carried through the aponeuroses from one side to the other, twice on each side, and anchored at various points with interrupted sutures The wound healed normally A plaster encasement, with walking-iron, was applied He was discharged January 18, 1942

Case 4—J H E, white, male, age 58, was admitted to the hospital, December 30, 1941, with a very extensive incisional hernia in the right upper abdomen, following a gallbladder operation two years previously There were five separate pockets in the hernial area

Operation—January 8, 1942 Two cutis grafts were used The first was taken from the redundant tissue in one of the wound flaps and was sutured to the posterior fascia and parietal peritoneum The remains of the fascia were sutured over this graft A second cutis graft, from the right thigh, was sutured to the aponeurosis surrounding the hernial opening The patient was discharged January 16, 1942

Case 5—I T, white, male, age 54, was admitted to the hospital, January 7, 1942, for repair of a large, right direct inguinal hernia

Operation—January 9, 1942 After the sac had been closed and the transversalis fascia sutured, a cutis graft was placed in position and sutured to the shelving edge of Poupart's ligament laterally, to the pubic periosteum at the lower end, on the medial side to the sheath of the rectus in the lower two-thirds and to the conjoined tendon in the upper third, a small notch was cut in the graft so as to make it fit loosely around the cord The aponeurosis of the external oblique was brought underneath the cord, and the undersurface of the aponeurosis was sutured to Poupart's ligament so that it would fit snugly over the cutis graft

CONCLUSIONS

Cutis may be used in all cases in which the use of fascia or tendon might be indicated, with the expectation of better results It heals in rapidly and well, has great vitality, is able to survive under adverse conditions, possesses great tensile strength, has a good blood supply, gradually assumes the function of the part it replaces, and is readily available

Its greatest value lies in the repair of large incisional herniae, also inguinal herniae with defective structures or those in which the structures cannot be brought into proper approximation without undue tension It is useful in bone and joint surgery, is suitable for the reconstruction of tendons, makes

excellent ligature and suture material, and is of value in filling out defects of contour in various parts of the body

NOTE The writer wishes to acknowledge the help and assistance of Dr Bankhead Banks and the hospital resident staff in the development of this method and in the care of these patients

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RETROVAGINAL HERNIA *

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RETROVAGINAL HERNIA and other defects in which there are changes in the normal anatomy and relationships of the pelvic floor and the cul-de-sac of Douglas have been discussed in the literature under the titles of posterior vaginal hernia, enterocele, cul-de-sac hernia, Douglas' pouch hernia, and high rectocele. Some of these conditions are not true herniae, and, therefore, the term retrovaginal hernia, applied to a definite entity which meets the requirements of a true hernia, seems appropriate and descriptive of the condition under discussion. Anatomically, it is characterized by the protrusion of a peritoneal sac through the cul-de-sac of Douglas which dissects its way between the vagina and the rectum and presents as a mass in the vagina. It is of rare occurrence.

This seems strange when one stops to consider the anatomy of the pelvic floor, which is composed largely of the levator and coccygeus muscles and their covering fasciae.

In animals who travel on all fours, the force of intra-abdominal pressure is exerted on the abdominal muscles, and the levator and coccygeus, or their comparable muscles, have the function of moving the animal's tail. In the human, the erect posture transfers to them the function of a pelvic floor.

This diaphragm is perforated by openings for vessels and nerves, and by larger openings for the urethra, vagina and rectum.

The superficial fascia of the pelvic floor extends onto, and is intimately connected with the urethra, vagina and rectum.

Derry³ has pointed out the fact that the levator is one of the most variable muscles in the body. Symington² states that the center of the pelvic floor averages one inch in thickness, whereas laterally it may attain a thickness of two or three inches. He thinks the vaginal opening is the main source of weakness but this is offset to some degree by the fact that the vagina passes obliquely from below upward and backward so that the general effect of intra-abdominal pressure is to force the anterior wall against the posterior.

Although this diaphragm is perforated at its thinnest portion in the midline by three large tubular structures whose lumina vary in size to accommodate the passage of material, hernia in this area rarely occurs.

The obliquity of the pelvic cavity which allows the force of intra-abdominal pressure to expend itself to some extent on the bladder, symphysis and anterior abdominal wall no doubt furnishes considerable protection to the pelvic floor.

The length of the mesentery of the intestine and the frequent presence of the sigmoid flexure occupying the cul-de-sac probably act to some degree in protecting the pelvic floor from intra-abdominal pressure in the absence of fluid or tumors.

* Read before the Southern Surgical Association, Pinehurst, N C, December 9-11, 1941

While most of the reported cases of retrovaginal hernia have occurred in women who have borne children, cases have also occurred in nulliparous women

The strain and trauma of childbirth thus assume considerable importance in the etiology, but some congenital defect must play an important part since the condition is so rare in multiparous women and occurs in those who have not borne children. Such a defect may occur in the muscular diaphragm or the fascia

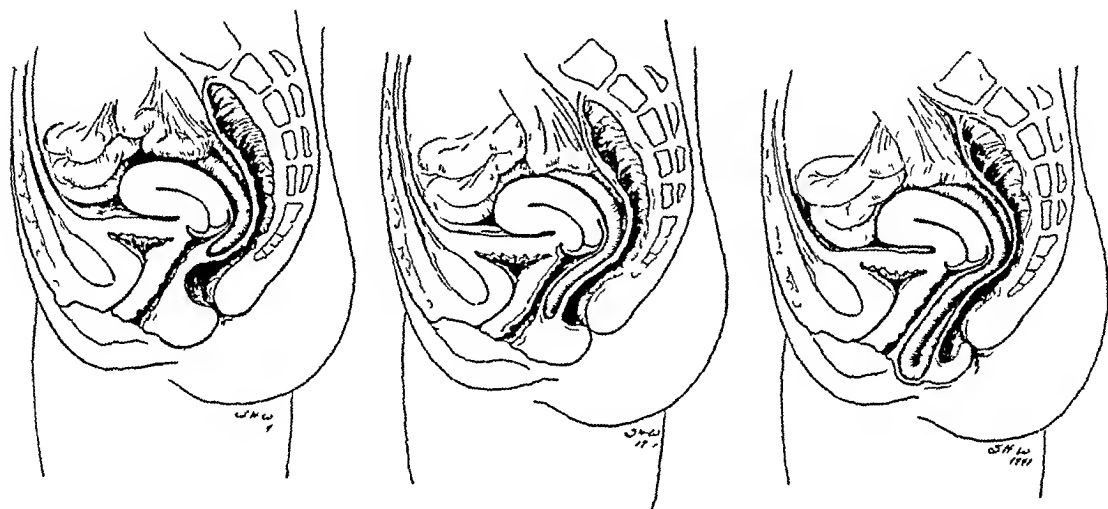


FIG 1—Varying degrees of herniation. This condition may occur with or without an associated rectocele

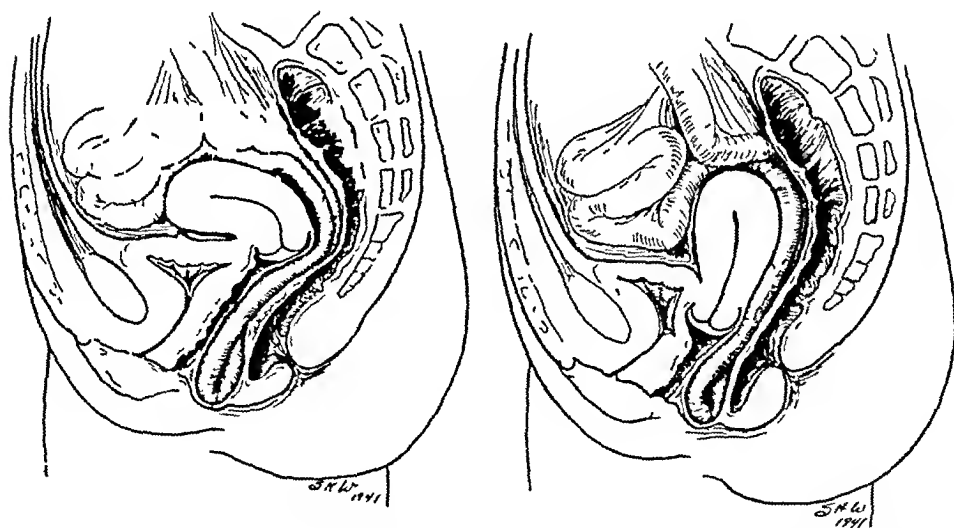


FIG 2—Postvaginal hernia may occur with the uterus in normal position or associated with varying degrees of prolapse

It is probably true, however, that even in the presence of such a defect a congenitally deep cul-de-sac is an important factor in the development of such a hernia

In the fetus, Douglas' pouch extends down to the levator muscles. It is gradually elevated during development until, at puberty, it is opposite the second or third sacral vertebra. If this elevation does not take place a congenitally deep cul-de-sac results

Blaisdell¹⁶ has described ligamentous bands originating on each side of the cervix at the insertion of the uterosacral ligaments, which extend downward and are attached to the vaginal vault. He calls them *ligamenta plica vaginalia*. They give support to the vaginal vault, and if congenitally absent or if injured during childbirth they allow the vaginal vault to sag and contribute to the formation of a deep cul-de-sac. Under such circumstances, should there be a defect in the muscles or fascia of the pelvic floor, conditions are present which predispose to retrovaginal hernia.

The strain and trauma incident to parturition, increased intra-abdominal pressure from fluid or tumors in the abdomen, or prolonged severe muscular effort might be the initiating factor in the formation of such a hernia.

There is a marked degree of confusion evident in the literature as to what properly constitutes a true retrovaginal hernia.

Hall,⁴ in summarizing a review of the literature on this subject, comments as follows: "Today there is complete disorganization in the literature and a lack of reliable statistical data on vaginal and pelvic herniae because of multiplicity and uncertainty in terminology and diagnostic requirements, and because of inadequate examinations and reports and mistaken interpretations to be noted in many writings."

Miles⁵ has noted this confusion and has proposed that all herniae through the pelvic floor should be classed as pelvic hernia with the point of egress denoted to give the subvariety of the hernia.

This follows the common usage with reference to hernia into the inguinal canal, where the terms direct and indirect denote the point of egress of the hernia from the abdominal cavity. Adoption of this suggestion would greatly simplify the problem of pelvic hernia.

Miles pointed out that cystocele and rectocele are spoken of as herniae, while neither meet the requirements of a peritoneal sac. They are merely prolapses of the anterior or posterior vaginal wall.

With reference to prolapse, he has the following to say: "In descensus or prolapse of the uterus accompanied by abdominal viscera bulging into the cul-de-sac, there is no true hernial sac and no ring or aperture through which the viscera herniate. The uterus descends because of stretched and attenuated cardinal and uterosacral ligaments. The cul-de-sac is enlarged and there is a descent of the pelvic floor. This condition is properly called, *elythrocele* or vaginal enterocele."

Cary and Young⁶ agree with this viewpoint and state that "A true posterior vaginal hernia is a definite peritoneal sac pushing down from the pouch of Douglas in the midline and dissecting between the rectum and vagina. The neck of the sac is located between the uterosacral ligaments just behind the top of the vagina, and through this abdominal contents pass to form a mass which may bulge out through the vulva when the patient strains down."

Sweetser⁷ reports a case in which he opened the abdomen, and presents a drawing showing an opening posterior to the uterus in the center of the

pouch of Douglas He says this was one inch in diameter and that the finger could be passed through the opening into the pouch below

Black¹¹ also has reported a case in which the neck of the sac only admitted the index finger

The importance of the deep cul-de-sac in relation to prolapse of the uterus has been emphasized by Jones,⁸ Potthast,⁹ and others

It is recognized that many of the failures following vaginal hysterectomy have been due to neglect in obliterating a deep cul-de-sac, and this step in the operation is now generally practiced Waid¹³ and Counseller¹⁴ have both emphasized its importance

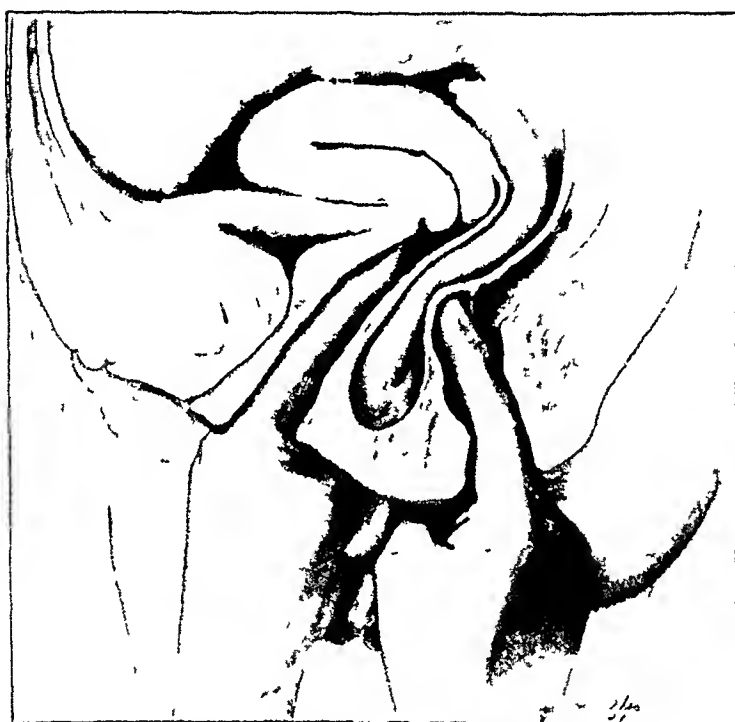


FIG 3—Examination with one finger in the vagina and one in the rectum is of the greatest diagnostic value in differentiating this condition from rectocele

Here, there is a downward pouching of the relaxed cul-de-sac which pushes the upper part of the vagina ahead of it, but there is no true sac dissecting its way between the rectum and vagina Such a cul-de-sac fails to qualify as a retrovaginal hernia

Prolapse of the uterus with sagging of the pelvic floor and a wide, deep cul-de-sac may be compared to marked diastasis of the recti muscles In this condition, there is a pouching of the abdominal wall lined by peritoneum, but no true neck or sac in the sense these terms are used in relation to other herniae

If Miles' criteria as to what constitutes a true retrovaginal hernia are accepted, a great many cases reported as such will have to be rejected

Hall⁴ accepts only 26 reported cases as fulfilling the requirements, while Cary and Young⁶ say that there are 70 authentic cases on record No doubt there are many unreported cases

The symptoms complained of by the patient are a sense of weight and pressure in the pelvis, and a variable degree of bulging into the vagina. Where the sac is well developed, a mass may protrude from the vagina on standing or straining, which usually disappears when the patient lies down.

Many of the reported cases had had previous operations for suspension of the uterus, or for plastic repair of the pelvic floor, with a recurrence of the bulging as soon as the patient got up. This is always suggestive of such a hernia.

Cases are on record where several plastic operations have been undertaken, with immediate return of the protrusion, and only when the true condition was discovered and treated was relief obtained. In these cases the rectocele had been cured but the hernia was unrecognized and promptly protruded after operation.

When a woman presents herself complaining of a vaginal protrusion, it is natural to think of the common causes of this condition, namely, cystocele, rectocele, or prolapsus. Unless vaginal hernia is borne in mind, and a search made for it, it may be overlooked.

If the mass contains intestine, peristaltic waves may be seen over its surface, and reduction may be accompanied by a gurgling sound. This is not present if the contents are omentum or fluid.

Examination with one finger in the rectum and one in the vagina will differentiate the condition from rectocele, which may coexist, as it will show that all the protrusion is not due to the rectocele. In cases where rectocele does not exist this maneuver helps to establish the fact that the protrusion originates behind the cervix, and if the patient is asked to strain it will determine the presence of abdominal contents in the protrusion.

The following complications have been discovered by Bueerman¹ in his survey of the literature (Table I).

TABLE I

Complications	No. of Cases
(A) Interference with delivery	10
(B) Hernia incised or excised because of error in diagnosis with death	3
(C) Pelvic abscess following delivery with spontaneous cure	2
(D) Rupture of hernia with evisceration and death	2
(E) Rupture of hernia with recovery	1
(F) Rupture of hernia during delivery with recovery	1
(G) Death from incarceration of hernia	1

In view of the small number of cases accepted by Bueerman as proven in his review, namely, 76, these figures prove the condition to be serious and accompanied by a rather high mortality.

The treatment is surgical. Palliation by pessaries does not afford relief as it does in some cases of prolapse, since a pessary cannot obstruct the hernial opening.

The same principles apply here that apply to the treatment of hernia elsewhere, namely, isolation of the sac, disposition of the sac, and closure of the point of egress of the hernia from the abdominal cavity.

There are two avenues of approach. The abdomen may be opened, the sac

inverted into the abdomen and disposed of, and the cul-de-sac obliterated by the Moschcowitz technic for the treatment of prolapse of the rectum. An abdominal approach may be necessary if abdominal contents are adherent in the sac, or if intra-abdominal pathology requires section.

In cases where this is not necessary, the vaginal approach is more desirable. This consists in opening the vaginal plate from the perineum to the cervix, dissection of the sac from the rectum and surrounding tissues, ligation of the neck of the sac, excision of the excess, anchoring the stump behind the cervix, and obliteration of the cul-de-sac by approximating the uterosacral ligaments. The remaining tissues are approximated and a high perineorrhaphy completes the operation. An occasional case may require both the vaginal and abdominal approach.

The following case seems to meet the requirements of a true retrovaginal hernia.

Case Report—Mrs J J U, white, age 52, housewife, para 4, gravida 5, was seen April 14, 1941. *Chief Complaint* Vaginal protrusion and soreness in lower abdomen. *Previous History* In September 1938, she had been operated upon for prolapse of the uterus by the Murphy technic. Following the operation she had soreness and pain in her lower abdomen and pelvis. The pain was at times sharp and cutting in character, and at other times dull, with a feeling that everything was dropping out of her. In April, 1939, she discovered something protruding from her vagina. This mass had become irritated and there had been a discharge purulent in character, at times streaked with blood.

The mass now protrudes from the vagina, becomes very sore, and causes her to curtail her activities, keeping her in bed a good deal of the time. When she lies down the mass recedes, and she is more comfortable. She takes enemata frequently. If she does not she says it feels as if the bowel gets into the protrusion and makes her uncomfortable. At times she has burning on urination and a feeling as if she had not emptied her bladder completely.

Physical Examination—Abdomen Transverse lower abdominal scar under which can be felt a tender mass, probably the halves of the uterus implanted in the abdominal wall.

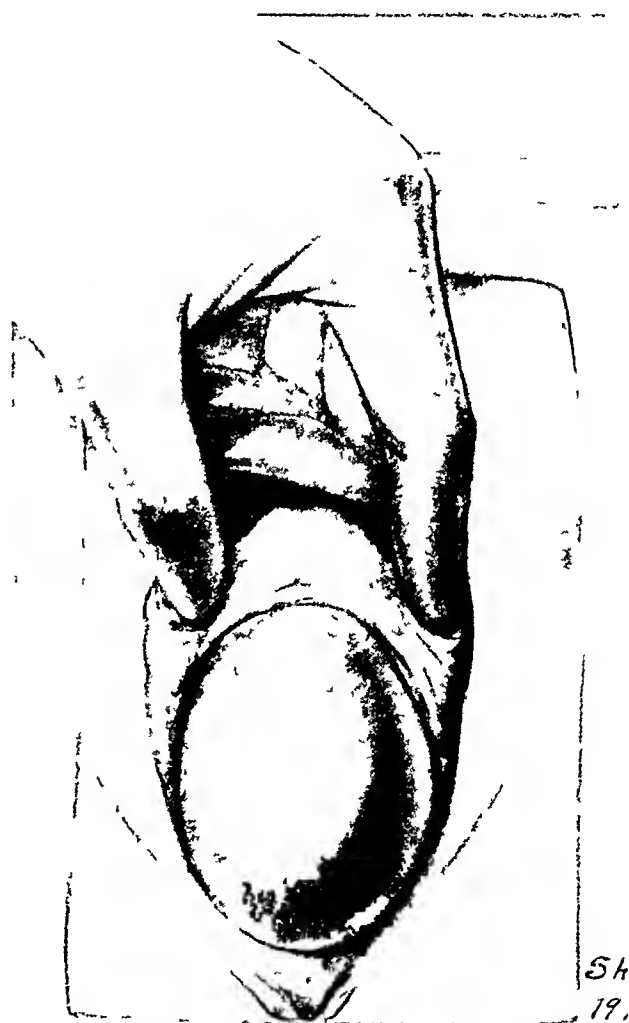


FIG 4—Appearance of the mass in the case reported, when the patient strained.

Pelvic Pains outlet Small cystocele, redundant vaginal walls When the patient was asked to strain, a mass as large as an orange appeared through the vulva with startling suddenness This could be easily reduced, and was accompanied by a gurgling sound With a finger in the rectum and one in the vagina it was apparent that the patient had only a moderate rectocele and that the mass was a hernia containing intestine The cervix was fixed high up in the vaginal vault

Operation—An incision was made from the cervix to the middle of the perineum, after normal salt solution with adrenalin had been injected under the vaginal plate The rectum was identified by passing a sponge stick with tonsil sponge into the rectum

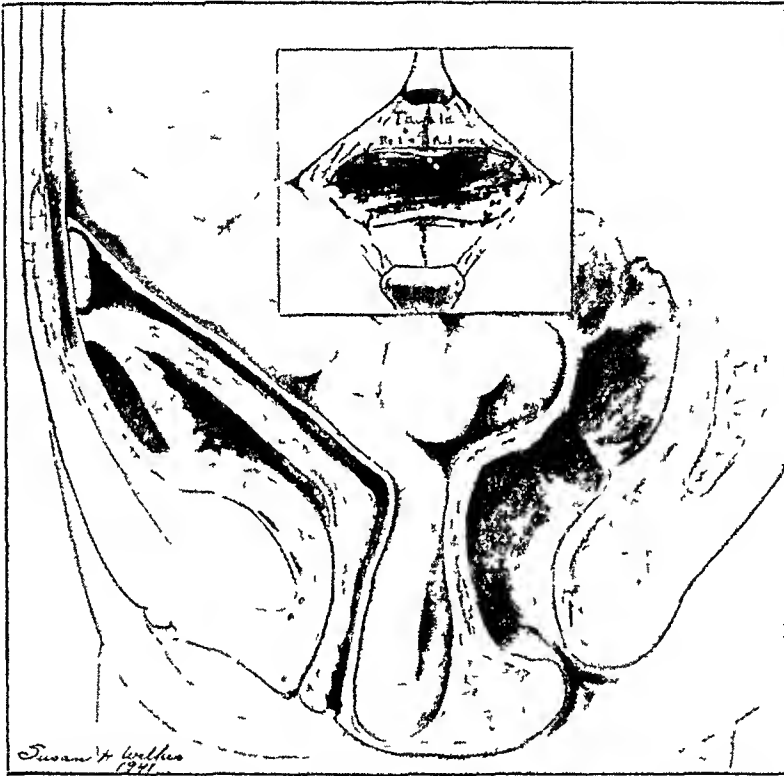


FIG 5—Condition present in the case reported. Inset shows the uterus sutured to the abdominal fascia according to the Murphy technic

The peritoneal sac was dissected loose from the rectum, and freed entirely from the vaginal plate and dissected up to the level of the ureterosacral ligaments at the cervix The sac was opened and a small amount of straw-colored fluid escaped This was evidently a pocket which had been shut off Another opening was made which entered the peritoneal cavity, and small intestine appeared in the wound The table was raised to a Trendelenburg position and the intestine pushed back into the cavity

The sac was ligated by a purse-string suture inside, and then by a suture outside of this suture, and the excess sac was cut off The stump of the sac was sutured to the posterior surface of the cervix The patient had had a previous suspension operation and it was impossible to pull the uterus down enough to identify the ureterosacral ligaments, but the tissues behind the cervix were brought together by interrupted sutures in an effort to obliterate the cul-de-sac A line of sutures was then placed approximating the fascia over the rectum The excess of the vagina was cut off, a high perineorrhaphy was performed, and the vaginal plate closed by interrupted chromic catgut sutures

A recent examination of the patient shows that there has been no recurrence and that she has been relieved

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ACUTE HEMATOGENOUS OSTEOMYELITIS*

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THE ADVENT of chemotherapy and revival of attempts to control severe staphylococcal infections by serum therapy have been partially responsible for renewed interest in the study of acute hematogenous osteomyelitis. Perhaps the greatest single impetus were reports suggesting that the long accepted teaching that the one great measure in the relief of the disease, to drill the bone and release the infection, was not only not helpful but actually harmful. While this question has remained undecided, numerous new advantageous measures have been introduced and added to our therapeutic armamentarium.

In this communication, a series of cases of acute hematogenous osteomyelitis are reported. The details of a group of 66 cases of the disease occurring at Charity Hospital, New Orleans, from 1937 through 1940, are given, and are compared with a series of 112 cases previously reported by one of us¹ from the same institution. The mortality for the more recent group was 66 per cent, and the mortality for the previous group of 112 cases occurring in the same institution between 1930 and 1936, inclusive, was 24.1 per cent. This great discrepancy in mortality represents an obvious improvement in management of the disease, and it was hoped by a detailed study of the two groups and comparison of their divergent methods of management that some facts could be culled which would help to establish the correct changes in therapy.

In studying these cases an attempt was made to review the records of only primary cases of acute hematogenous osteomyelitis. By this is meant cases which were not operated upon elsewhere and cases not in a chronic stage. They were considered primary acute hematogenous osteomyelitis even though the disease had been present for two weeks, provided the symptoms were acute and they had not been operated upon. Only hematogenous osteomyelitis was included. Traumatic osteomyelitis resulting from compound fractures and osteomyelitis by continuity from some local infection was excluded. In addition to this, recurrent cases of acute hematogenous osteomyelitis were excluded even though the disease had apparently healed and recurred locally.

Osteomyelitis is common, but acute hematogenous osteomyelitis, restricted to primary cases, may be found surprisingly uncommon, even rare. The impression that it is more common than it is probably comes from the fact that recurrences are so numerous and that reported series usually contain these recurrences.

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Even in a large institution like Charity Hospital in New Orleans, where from 1937 to 1940 there were 237,105 patients actually admitted to the hospital beds, only 66 cases of primary acute hematogenous osteomyelitis were found. This represents one patient with acute hematogenous osteomyelitis in every 3,592 patients. In the previous series from the same institution, the incidence was one case in 3,490 patients admitted.

Negro children have the disease relatively less frequently than white children. Fifty-one (77.3 per cent) of the 66 cases in this second series were white patients and in the same period, approximately 55 per cent of the total admissions were white patients. A similar variation in the incidence of osteomyelitis in Negro and white patients was reported in the previous series.¹ A possible cause for this difference is the greater susceptibility of the white race to skin infection and thus staphylococcal infections in general. This is a casual observation for which we have no conclusive proof. Boils, frequently seen in white patients, are relatively rare in the Negro race. Fourteen (21.4 per cent) of the 66 patients in this group gave a history of boils either immediately before or concomitant with the onset of acute hematogenous osteomyelitis. All of these 14 patients were white patients.

The more frequent occurrence of the disease in the male is again shown in this study. Forty-four of the patients were males and 22 were females. The explanation for this greater susceptibility in boys has repeatedly been stated to be the trauma factor. Possibly, also, there is variable incidence of dermal infection in the two sexes.

Trauma was mentioned as a casual factor in the records of 24 cases (36.4 per cent), probably too high a figure to be merely a coincidence. The disease with its prolonged morbidity is so severe, that it would not seem incorrect to recommend partial inactivity for children with furunculosis, if only to avoid such a serious even though unlikely complication as osteomyelitis.

Acute hematogenous osteomyelitis is predominantly a disease of growing years. The mean-age in this series, as in the previous one, was nine years. True hematogenous osteomyelitis is very rare in adult life, and apparently runs a shorter, milder course. The mean-age for the patients who died was seven years, a slight shift under the mean-age of all patients, which possibly indicates a higher mortality among younger children, but primary acute hematogenous osteomyelitis is serious at any age.

Symptomatology and Clinical Course—No attempt will be made to discuss fully the symptomatology or clinical variations of the disease, but a few important features of symptomatology, impressed upon us by our findings in this study, are herein noted. The statement that acute hematogenous osteomyelitis is not always easy to diagnose may be surprising, but it is accurate. The onset of the disease is usually sudden but it may not be fulminating. Sometimes a period of malaise, with mild pain in the region of a joint, may precede graver manifestations of the real trouble. It is very likely that in these instances parents do not realize how sick their inactive child is. Temperatures in many instances are not taken and recorded. The fact that patients

may later develop most intense signs of septicemia, after the initial symptoms were mild pain, a limp, and low grade fever, would seem to indicate that the septicemia in these cases originates slowly from the secondary focus of infection in the bone and not as a manifestation of a probable haphazard and sporadic bacteremia from an original infection such as a furuncle. The temperature rises gradually or abruptly, usually to 102° to 104° F. A chill is not uncommon but it does not occur as a first symptom. In three instances in the 66 cases convulsions were recorded. They are the result of fever in young children.

The local symptom, initially, is pain and pain alone. At the onset pain may be mild but as the disease progresses it may appear to be excruciating, particularly in young children. It is generally in the region of the joint. The patient resents any movement of the involved extremity. The pain is usually well localized but it may be diffuse and poorly localized, causing great confusion as to the exact site of the disease, particularly when it involves the upper end of the femur or the ilium. Pain may involve the whole thigh when the disease is in the region of the hip joint, and because movement of the knee results in severe pain, localization of the disease may erroneously be judged to be low in the femur. In these instances palpation of the thigh at any area may result in excruciating pain. This is undoubtedly due to radiation of the pain from the region of the hip as frequently occurs when lesions are localized there. The exact location of acute hematogenous osteomyelitis in the region of the shoulder joint may likewise be confusing. These are very significant facts because in the early stages of the disease, the only points on which to make a diagnosis of acute hematogenous osteomyelitis are the pain and high fever subjectively, and the tenderness objectively. Swelling, redness, heat and induration of soft tissues may make their appearance as the disease progresses. Roentgenograms, as will be seen later, are not helpful.

Every early feature of acute hematogenous osteomyelitis may be present and the disease subside without the bone ever showing changes. In such a case the bone might be drilled since the usual indications for the diagnosis at that stage are fulfilled. Too much haste in such an instance may convert a subsiding periostitis into a prolonged osteomyelitis. We have observed three such cases. The temperature chart of one is shown in Chart 1.

Rapid pulse and other signs of sepsis may be expected including stupor, irrational states, and coma in more severely ill patients. Occasionally another bone, another organ, or the subcutaneous tissues may be the seat of metastatic lesions. In one patient in this series an eye was lost because of metastatic abscess and in another instance a severe acute subcutaneous infection in the region of the buttocks occurred. Pneumonia, empyema, pericarditis, and pathologic fracture, are also complications observed in this group of cases.

Roentgenologic Evidence—In studying these cases in detail and also in the previous group, it was found that there was no uniformity in appearance of positive evidence of acute hematogenous osteomyelitis in roentgeno-

grams Roentgenograms were negative during the first week of the disease in all cases except three. In one instance the roentgenograms showed osteoporosis after the disease had been present for four days only. In two more cases osteoporosis was present on the fifth day of the disease. In many cases roentgenograms remained negative as long as 8, 9, 10, and even 14 days, to become positive later. Usually there is appearance of some evidence of the disease in the bone on roentgenograms taken between the eighth and tenth day of the disease. The first significant sign is usually a slight osteoporosis in a small circumscribed or diffuse area (Fig 1), and/or



FIG 1—Roentgenograms taken on the eighth day of the disease and eight months after onset. The earliest sign of the disease is slight osteoporosis as indicated by the arrow. Drainage only of an abscess was undertaken. This child, age 10, ran a very severe course. The osteomyelitis, as indicated by the subsequent roentgenograms, spread through osseous tissue, without elevating the periosteum. Recovery.

evidence of elevation of the periosteum. The roentgenograms, of course, serve as valuable evidences of the progress of the disease—its dissemination through the bone, the appearance of sequestra, and finally the marks of healing, the reappearance of calcium density, and sclerosis, with disappearance of osteoporotic areas (Fig 2). Evidences in the roentgenograms indicate that the osseous spread of the disease is very rapid. Though the first roentgenograms taken may show a very small area of osteoporosis, those taken on the eighteenth and twenty-first days of the disease usually show the full spread of the disease. Roentgenographic evidence may rarely indicate a continued spread of the disease for several weeks after that. The full extent of involvement is probably usually present early on the eighth day, even when only a small area is noted roentgenographically. The fundamental changes have taken place and decalcification continues for days there-



FIG. 2—Roentgenograms and final healed result in a case in which osteotomy was performed on the fifth day of the disease. There was a marked elevation of the periosteum in contrast to the appearance shown in Figure 1 but no sequestrum formed & sinus resulted necessitating a subsequent osteotomy a year and one half after onset. The diffuse recalcification is a good example of how healing appears after the disease has subsided.

after, manifesting roentgenographically the full area involved between the end of the second and third week. No definite evidence of demarcation of the sequestra can be found in the roentgenograms before the fourth week of the disease. Sometimes evidence of a sequestrum is not present in the roentgenogram until the second or third month of the disease. In some instances evidences of sequestra never become apparent roentgenographically.

Further evidence of a surprising nature is found in the roentgenograms. Even though the disease may be clinically very severe, the area of osteoporosis may be relatively restricted (Fig 3). A comparison of roentgeno-



FIG 3—Roentgenographic appearance of the process one month after onset and eight months after onset. On admission, the temperature was 104°F, and the child was very sick. No drainage and no operation was undertaken. In spite of this there was a minimum spreading of the disease and recovery took place in eight months. This is one proof that factors determining the extent of spread are not influenced by surgical intervention. It is not proof that surgical intervention should not be employed.

grams and the time of operative intervention upon the bone shows there is no strict relationship between the operation and the extent of spread of the disease in the bone. In a case where an operation is not performed or is withheld for days after the onset of the disease, the disease may remain localized to a small area in the bone. On the other hand, the disease may spread widely throughout the bone even though roentgenographic evidence was negative at the time an osteotomy was performed (Figs 2 and 4). The spread of the disease in the bone is probably determined by the extent of vascular involvement, the retrograde thrombosis, and the balance of bone immunity to infection virulence and not to pressure. These facts contend severely with the usual impression that the spread of the disease may be countered by an early operative procedure. They do not, however, prove that an early operative procedure is not of value and is not indicated.

Localization of the Disease—A single bone was involved in 57 cases. Multiple bones were involved in nine, or 13.8 per cent of the 66 cases (Fig 6). The incidence remains surprisingly high, and coincides with the percentage of multiple bones involved in series reported by other authors (Wilensky²).

A total of 76 bones involved were found in the 66 patients, in seven, two bones were involved, and, in two, three bones were involved. The time or occurrence of the metastatic lesion is usually early within the first week of the disease but a secondary bone may become involved even years later. The bones involved are shown in Table I. The disease involves most frequently the metaphyses of bones with the fastest growing epiphyses. Thus, the lower end of the femur, the upper end of the tibia, the upper end of the femur are places of predilection for osteomyelitis. Next in frequency the metaphyses of bones of the upper extremity are found involved. Pelvic bones are not infrequently involved, but the ribs, spine, and head, are usually not the seat of true, acute hematogenous osteomyelitis.

TABLE I
THE RESULTS OF BLOOD CULTURES
ACUTE HEMATOGENOUS OSTEOMYELITIS

Blood Cultures in 66 Cases

Taken	36	
Positive	20 (one death)	{ Staphylococci 18 (90%) Streptococci 2
Negative	16 (44.4%)	
Staphylococcal septicemia and osteomyelitis—18 Cases—one death—(5.5%)		
Longest continuation of positive cultures—10 days		

Pathology and Pathogenesis—The usually accepted view of the pathogenesis of acute hematogenous osteomyelitis, is the one advanced by Starr,^{3 4} who gave as evidence for his conclusions of the pathogenesis, the necropsy findings in a child, age two, who died of septicemia 48 hours after the onset of symptoms. Careful examination showed the infection in the bone to be just above the epiphyseal line, and for a comparatively small extent the periosteum was elevated in that region. The gross appearance showed inflammation localized to this region. He argued that infection usually beginning in the end-arteries of the metaphysis spread along the epiphyseal plate to the subperiosteal region, where it progressed, raising the periosteum around the shaft of the bone. Many arguments concerning therapy are based upon this conception of the pathogenesis. Now, in reality, it is far from proved. Careful study of the roentgenographic appearance of the disease in different cases, and at different stages, does not always bear out the idea that the inflammation spreads thus. There is some reason to believe that in certain instances the disease begins under the periosteum and spreads into the bone. Roentgenographic evidence of this is a small area of osteoporosis in the subperiosteal region and clinical evidence is the discovery of subperiosteal but not intramedullary pus (Crossan⁵). In other instances, roentgenographic evidence may indicate that the disease begins in the cortex at some distance from the metaphysis, that it spreads through the bone as an osseous cellulitis with or without elevating the periosteum. The periosteum does not always have to be elevated even when severe osteomyelitis is shown roentgenographically (Fig. 1). Brodie's abscess may be regarded as an abortive form of acute

hematogenous osteomyelitis It is usually at some distance from the epiphyseal plate and the spread from such an initial focus in the cortex, if not aborted, may presumably be in both directions The rapid spread of the acute infection with elevation of the periosteum, thrombosis of the artery, and sequestration of a large segment of the shaft, is rarer, in reality, than diffuse osteop-

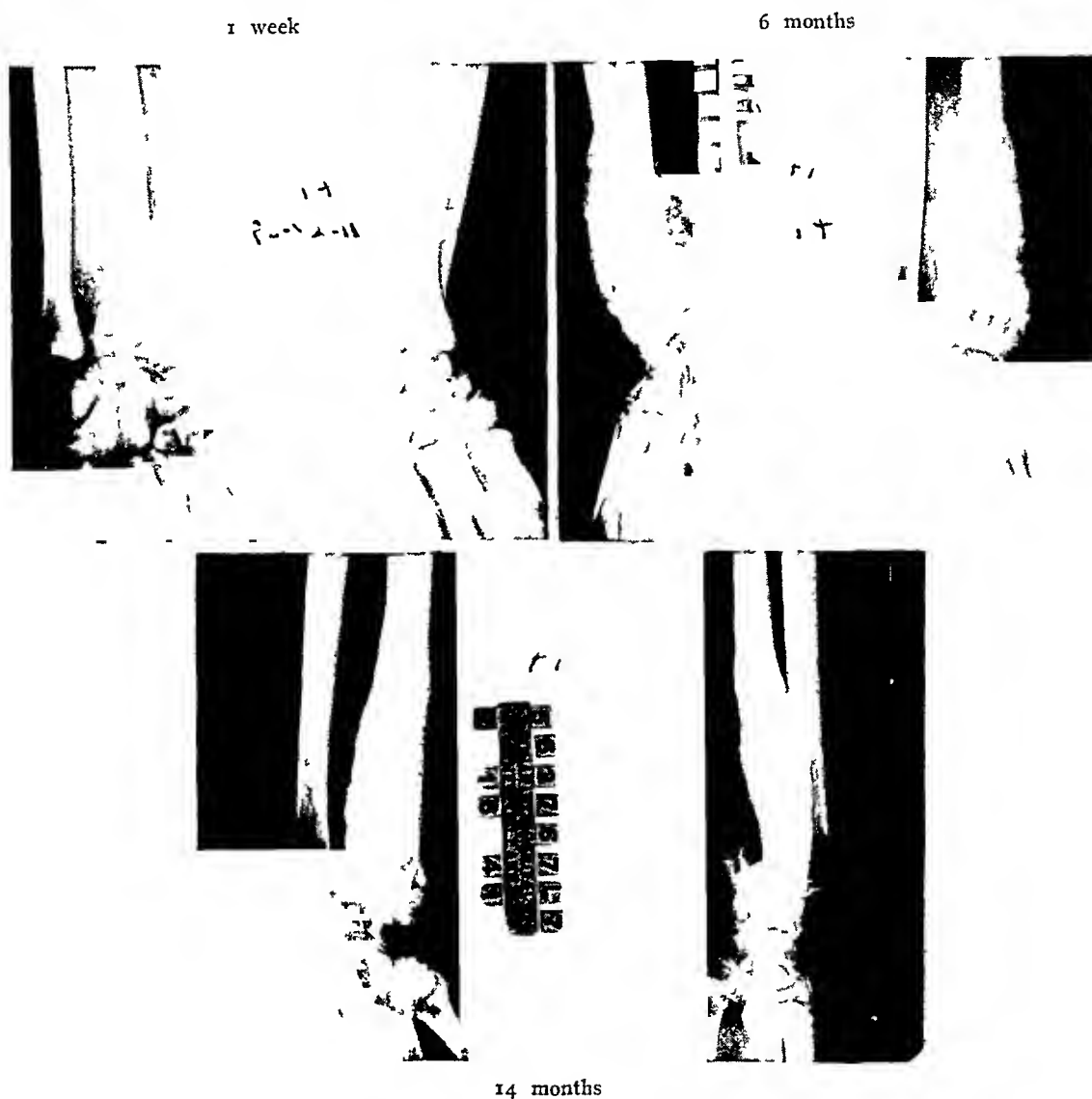


FIG 4—A window was put in the bone on the eighth day of the disease. A massive involucrum formed. A sequestrectomy was performed on two subsequent occasions. The child was clinically well one year after onset. In this instance the primary seat of the disease was in the diaphysis.

osis occurring in the shaft with a low-grade periosteal reaction and gradual thickening of the periosteal part of the acutely inflamed bone, which the usual concept regards as necrotic.

One feature of the pathology and pathogenesis of the disease, so far insufficiently emphasized, is that it is a *vascular disease or an intravascular one*. The most pronounced features of it are due to the fact that the etiologic factors responsible for the systemic symptoms and the changes in the bone are initially in the vessels. If one were to base therapeutic indications on pathologic conception, instead of on careful studies to evaluate the measures,

it would seem just as sound, or more so, to advocate ligation of a vein leading from that particular bone than to drill the bone with the hope of freeing pus or of hitting that particular nidus of infection which is intravascular and which is liberating organisms into the systemic vascular system

Sequestration does not always take place in acute hematogenous osteomyelitis. At least, it cannot always be demonstrated roentgenographically nor at operation (Figs 1 and 5). In such instances the bone is diseased and in-



FIG 5—Roentgenograms show the appearance of the bone one month after onset and seven months after onset. No operation was performed. There was no drainage. The patient made an uneventful recovery and was well in ten months, active and playing. There was a massive periosteal thickening surrounding the old bone and thus the meaning of sequestrum becomes obscure. According to the usual concept it is a dead obnoxious piece of bone with the implication that it must be removed before recovery ensues. Sequestra in hematogenous osteomyelitis are probably almost always viable.

flamed, though viable. What is regarded as sequestration itself may not be actual necrosis. Instead of sequestration being the result of elevation of the periosteum and cutting off the blood supply by gradual pressure increase due to pus, it may, theoretically, be the result of sudden thrombosis of an artery leading to a particular segment of the bone.² Sequestration, when it occurs, is usually a localized, rather small process, and, fortunately, does not often involve the whole shaft or a large length of the shaft of any bone.

In its chronic stage, osteomyelitis cannot always definitely be attributed to a sequestrum keeping up the infection. The recurrence of the infection in a bone, after it is once healed, may manifest itself as a reddish, tender inflamed area in the skin. Roentgenograms taken at this time sometimes show an osteoporotic area surrounding a firmly calcified sequestrum. It is just as common to find a diffused, thickened, ebony bone showing no definite location of the infection in the bone itself. In these instances even exploration,

with osteotomy, may not show a definite sequestium. It is conceivable that a reduction in the circulating staphylococcal-immune bodies may permit a dormant group of organisms to blossom again into an infection which is in viable bone and is not associated with necrotic bone.

Ciessman and Blalock⁶ have shown, experimentally, that sequestra may be absorbed or revitalized *in situ*. The question now arises as to whether the apparent sequestium is in reality ever completely dead bone. What is a sequestrum becomes a very important question. Certainly, under our old concept of the pathogenesis and the indications for treatment, it was regarded as something very obnoxious, which must be gotten rid of before the patient is well. These facts and clinical cases, herein reported, showing healing of osteomyelitis without ever having drainage, raise a doubt as to whether that conception is accurate.

Blood Cultures—The significance of blood cultures in acute hematogenous osteomyelitis is not clearly established. Baker and Shands⁷ found that 70 per cent of patients with acute hematogenous osteomyelitis, with proven staphylococcus septicemia, died and, with this as a basis, urged the efficacy of staphylococcus antitoxin since its use in a similar group resulted in only 25 per cent mortality. The mortality for staphylococcus septicemia was not found to be so high

in our series. Blood cultures were taken and were reported on 36 of the 63 cases. Out of the 36, 16, or 44.4 per cent, were negative, leaving 20 cases of acute hematogenous osteomyelitis with proved septicemia. One, or 5 per cent, of these patients died. Eighteen of the 20 positive cultures showed staphylococci (Table I). One of these was the patient who died (5.5 per cent mortality for staphylococcal septicemia). Six of these 18 cases with staphylococcal septicemia were treated with antitoxin, leaving 12 cases not so treated, with one death (8.33 per cent mortality for staphylococcal septicemia and osteomyelitis untreated with antitoxin). Unfortunately, blood cultures were not requested or not taken in three other fatal cases and in 27 other survivors.

Acute Hematogenous Osteomyelitis

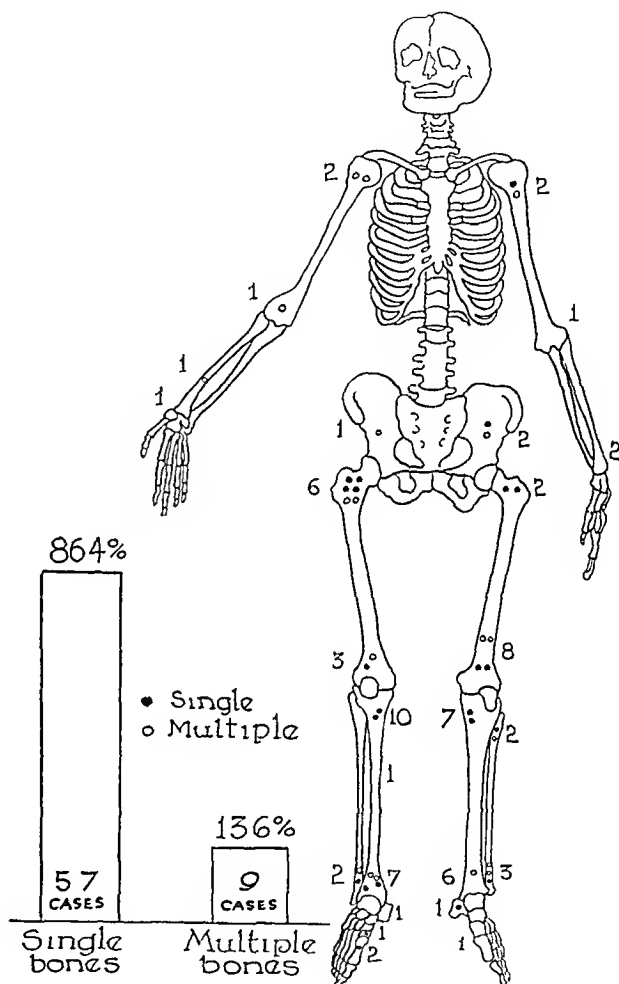


FIG. 6.—Illustrating the distribution of acute hematogenous osteomyelitis in 66 cases, with a total of 78 bones involved.

In studying these cases it is apparent that repeatedly positive cultures do not necessarily give a bad prognosis. In one case, cultures remained positive over a period of ten days, the highest number of colonies reported per cubic centimeter being 20. Most of the cases showing positive cultures had only one culture taken. In this study, at least, staphylococcic septicemia

OPERATIONS PERFORMED

	DAYS AFTER ONSET																
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1	2 L	3 L	3 L	6 L	7 L	6	7 L	2 L	1 L	3 L		1 L		1 L		1 L	1 L
2			2 D	2 D	2 D	3 D	4 D	1 L	1 L					1 D		1 L	2 D
3				1 L	3 L	5 L	1 L		1 D	1 D					1 D		
4							1 D		1 L			1 L					
5						1 L			1 L								
6										1 L				1 L			
7									1 L								
8									1 L								
9																	
10																	1 L
11																	
12																1 L	
13																	
14																	
15																	

Mortality
32.5%
1st 48 hrs

57 operations, 20 deaths 35% 15 operations 2 deaths 13.3% 30 operations, 4 deaths 13.3%

Key "L" patients living, "D" patients who have died

FIG 7—The living and dead patients in the first group of 112 cases, arranged according to the days after onset of the disease on which they were operated upon and according to the days in the hospital before their operation was performed. The mortality in the first 48 hours was 32.5 per cent. The mortality between the third and seventh day of the disease was 35 per cent. In spite of this operation itself may not have been responsible for this high mortality but failure to prepare the patient properly before operation most certainly was a big factor.

did not prove to be as lethal as it may have been found to be in previously reported series, and certainly not as vicious as the factor or factors responsible for the astounding mortality in our first series. The mortality for cases with positive cultures in the first series, 1930-1936, was 50 per cent. Perhaps, to explain the high mortality for acute hematogenous osteomyelitis, one will have to look for other causes, some of which might have been masquerading under the guise of a helpful measure.

Operative Procedures—The fact that over 40 surgeons performed the operations upon these patients is obvious enough reason for expecting a variety of opinions and operative indications. In the first group studied, 71.4 per cent of the patients were operated upon within 48 hours, and in 90 per cent of these the bone was opened (Fig 7). In this group of 66 cases, 56 were operated upon. The remainder had no operations, and of these ten, two died. Single operation was performed on 28 patients (19 incisions and nine osteotomies). Multiple operations were performed upon 26 patients (72 operations) (Table II).

TABLE II
ACUTE HEMATOGENOUS OSTEOMYELITIS

66 Cases—Operations Performed		
Single Operations—28 Cases		
Multiple Operations—26 Cases (72 Operations)		
Operations within 48 hours—24 (osteotomy 18)		Deaths
Operations after 48 hours —32		1
No Operations —10		2

Twenty-four, or 36 per cent, were operated upon within 48 hours of admission (71.4 per cent in the first group). One of these, or 4.2 per cent, died. Eighteen, or 75 per cent, of this group of 24 cases had the bone opened at the first operation.

Twelve cases had no operations on first admission, two died. Three were aspirated, only one was subsequently incised, one had a subsequent operation upon the bone, with saucerization, ten, including the two deaths, were not operated upon.

Early operation upon the bone did not always result in prompt subsidence of systemic signs of sepsis (Chart 2), nor, as has been stated in discussing roentgenographic features, in limiting the spread of the disease in the bone. The systemic reaction in acute hematogenous osteomyelitis is usually prolonged, with or without drainage (Chart 3), but may subside promptly (Chart 4) even though the bone shows definite roentgenographic changes.

Wound Culture—Cultures were reported from the wound in 46 of the 66 patients. Forty-one of these were reported as positive. The organisms found were *Staphylococcus*—39, *streptococcus*—3 (one in mixed culture), and *Escherichia coli*—one (in mixed culture with *staphylococcus*).

Usually when blood cultures were taken the contaminant in the wound cultures was found to coincide with that in the blood stream. No particular therapeutic significance can be found in the wound cultures if blood cultures are available and reported positive. In the absence of positive blood cultures, however, cultures from the wound may be very significant in directing the type of therapy.

Mortality—In the entire series of 178 cases, 31 patients died, a mortality of 17.4 per cent. More interesting is the comparative mortality for the cases in the first group (from 1930 to 1936, inclusive) and that for the second series of 66 cases, from 1937 to 1940, inclusive. In the latter group the mortality was 6.6 per cent (four deaths in 66 cases), in contrast to the astounding mortality of 24 per cent for the previous group studied (1930–1936).

In the first group, 107 of the 112 cases were operated upon. In 77 patients the operation was performed within 48 hours after admission. In the group operated upon within 48 hours the mortality was 32.7 per cent. In relationship to the duration of the disease, the mortality was also high when operation was performed between the third and seventh day. The reduced mortality, concomitant with fewer emergency operations and less radical operative procedures, is no indication that operation was responsible

for the mortality. It does indicate that operation alone will not save patients, and that other measures probably deserve credit for the improved mortality. Pemberthy's and Weller's⁸ series of 19 cases, with no deaths, all of which had osteotomy performed soon after admission to the hospital, shows that early and radical operation is not only consistent with, but may be essential for, the lowest possible mortality. On the other hand Hoyt, Davis and Van Buren⁹ reported that without any operative procedure eight patients recovered with no deaths in the series. Only one had a residual draining sinus.

RESULTS

Attempts were made to estimate the final results. Information was gathered on 42 of the 66 patients in the recent series. Only 18 out of the entire group were personally observed and examined during the summer of 1941. The remaining estimate of the final results up to that time was obtained from letters or from the Out-Patient Clinic charts. Eleven cases are reported by letter. A summary of the results, during the summer of 1941, is as follows: Actually healed—20 out of 66 cases (Fig 8). The average time required for the patient to be well in these 20 cases was 17 months.

In an attempt to disclose the methods of value in the healed cases, and to elucidate the comparative value of measures used, 20 followed, healed cases were studied for procedures employed. In 14, osteotomy had been performed, in seven, incision and drainage only, and in one, no operation had been undertaken. In 31 cases in which the bone was opened, 14 (45 per cent) were well. Of 25 patients upon whom operation included incision only, seven (28 per cent) were well, and of ten patients who had no operations, two (20 per cent) were well. Though these figures are suggestive that osteotomy offers a shorter morbidity, they should not be accepted as conclusive. The time factor is not computed, and the conservative procedures have been used in a higher percentage of more recent cases. Only one case treated without operation could be traced. At least three were presumably well.

Plaster encasements, worn by 34 patients, about whom information could be obtained regarding the length of their use, showed that the average length of time an encasement remained on was 11 months. This only includes patients who are not still wearing plaster encasements. The length of time drainage continued in healed and unhealed cases was computed from information obtained on 35 cases. This was found to be an average of 19 months and four days.

Acute Hematogenous Osteomyelitis 66 cases 1936-1940

Summary of Therapy 20 Healed Patients

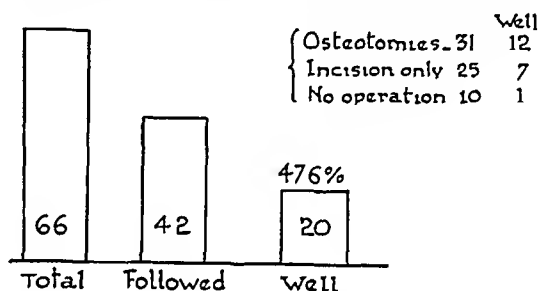


FIG 8—Graph showing results of follow up study. Only one patient in the no operation group was definitely followed. From latest information, at least three are believed to be well.

Chemotherapy and Antitoxin—Sulfathiazole was administered in 13 cases. In eight of these the blood culture was positive for staphylococci, of the remaining five cases the wound culture showed staphylococci in four. The wound culture was not reported in one case. These cases represented those in the latter part of the series, when the efficacy of the use of sulfathiazole for staphylococcal infections was more firmly established. One of the patients to whom sulfathiazole was given died. This patient was admitted two weeks after the onset of the disease, in an extremely critical condition.

The administration of sulfathiazole is not to be accepted as a "cure all." Even though the level may be above 7 mg %, the blood culture may be positive (Case 49, which died). Blood cultures may remain positive over long periods of time, even though sulfathiazole is being administered (Case 69). The culture was still positive after ten days, though both sulfathiazole and staphylococcal antitoxin had been administered. The highest blood sulfathiazole level recorded in this case was 4 mg %. The persistence of positive blood culture may be good evidence for vein ligation.¹⁰ Sulfathiazole administration, certainly, does not result in any rapid drop in temperature, such as sometimes dramatically occurs after the drainage of an abscess in this disease or after immobilization in a plaster encasement. Its value, however, remains undisputed in staphylococcal infections. Sulfathiazole locally in the wound was not employed in any of these cases. Its use thus is undoubtedly rational.

Antitoxin—In six cases, staphylococcal antitoxin was employed. In none of these instances did death result. The conclusions from such a small group, admittedly, are not valuable. In one instance, in which no other measure, such as drainage of an abscess, would account for it, the temperature fell dramatically after antitoxin was administered. On the other hand, the temperature was sustained until an abscess was drained in another patient, to whom antitoxin had been administered in adequate amounts. Out of six cases, in which antitoxin was given, five had sulfanilamide or sulfathiazole, or both.

The usual method of administration of antitoxin is to check the patient for sensitivity and desensitize if necessary. Then 10,000–20,000 units of antitoxin are given in an intravenous infusion. The next day 20,000–60,000 units are given in an infusion. The administration is repeated in a period of 12, 24, or 48 hours, as clinical symptoms indicate. A total of 200,000–1,000,000 units may thus be administered.^{11, 12}

In one case, staphylococcus toxoid was administered. This patient also received antitoxin at another stage of the acute process. Longacre¹³ has reported encouraging results for the administration of staphylococcus toxoid to patients with staphylococcal infections. It is rational and may prove of great value, particularly in the chronic case, with an acute recurrence.

Although no deaths occurred among the patients treated with serum therapy, no definite conclusions should be drawn from its effectiveness. At present it can be considered as a safe adjuvant therapy, with evidence accumulating for its efficacy.

SUMMARY OF TREATMENT

In the study of these 178 cases of acute hematogenous osteomyelitis, obviously, certain convictions and impressions are gained as to the best method of treating the disease. The cases were carefully studied in an attempt to evaluate the best measures or combination of measures to employ. Conclusions were not always possible but some impressive information was obtained. More attention was paid to therapy for the disease in the acute stage, when it was primary and first came to the attention of the physician or surgeon. Less definite study has been given to the operative indications in the late or chronic stages of the disease.

The following are fundamental measures of great value in the therapy

(1) Hydration and Electrolyte Replacement—The basis of all treatment for acute hematogenous osteomyelitis must be an attempt to keep the body in physiologic balance. These patients are very sick, and are usually dehydrated. They lose fluids by vomiting and excessive perspiration as well as through other channels. These fluids must be replaced. On admission, after the preliminary check, an infusion of dextrose, 5 per cent, in normal salt solution, should be started. The administration of fluids and electrolytes should be guided by physiologic principles, depending on the age and size of the patient.

(2) Protein Replacements—Extremely sick patients do not have an adequate protein intake, increased metabolism results in destruction of tissues, hemolytic organisms destroy blood cells, and severe anemia may advance rapidly. The replacement of blood cells and proteins in acute hematogenous osteomyelitis by repeated transfusions is the second fundamental for all therapy. Transfer of immune bodies into the recipient occurs. In this study, many more transfusions were administered in the second series of cases than in the first. Transfusion should be repeated daily, every other day, or every third day, depending on the severity of the infection and the condition of the blood. Transfusions may be small (100–200 cc) or they may be large (500 cc or more), depending on the age and size of the patient. The frequency and quantity of transfusion must be determined in the individual case, but it is absolutely essential to be constantly thinking of transfusion as a basic necessity in the disease. In this way, as the requirement for it arises, it will not easily be overlooked.

(3) Chemotherapy—Chemotherapy has had ample proof of its value. In the absence of a positive culture, since most hematogenous osteomyelitis is due to staphylococci, it is reasonable to start the administration of sulfathiazole. Immediate cultures should be taken to verify the rationality of the type of chemotherapy employed. If streptococcus is the proved organism in blood culture, sulfanilamide may replace the administration of sulfathiazole. Sulfathiazole should be administered to children in daily doses of 0.2 Gm per Kg body-weight (up to 20 Kg). Administration may, of necessity, be by intravenous infusion, in a 5 per cent solution, giving 0.06 Gm for each

Kg body-weight in 24 hours During the administration of chemotherapy it is essential to watch the daily blood count and to watch the level of the drug in the blood stream

(4) Immunotherapy—Two recent advances, which may prove of great help, in the treatment of acute hematogenous osteomyelitis are staphylococcus antitoxin and staphylococcus toxoid Very convincing experimental evidence has been advanced for the employment of antitoxin Baker and Shands,¹¹

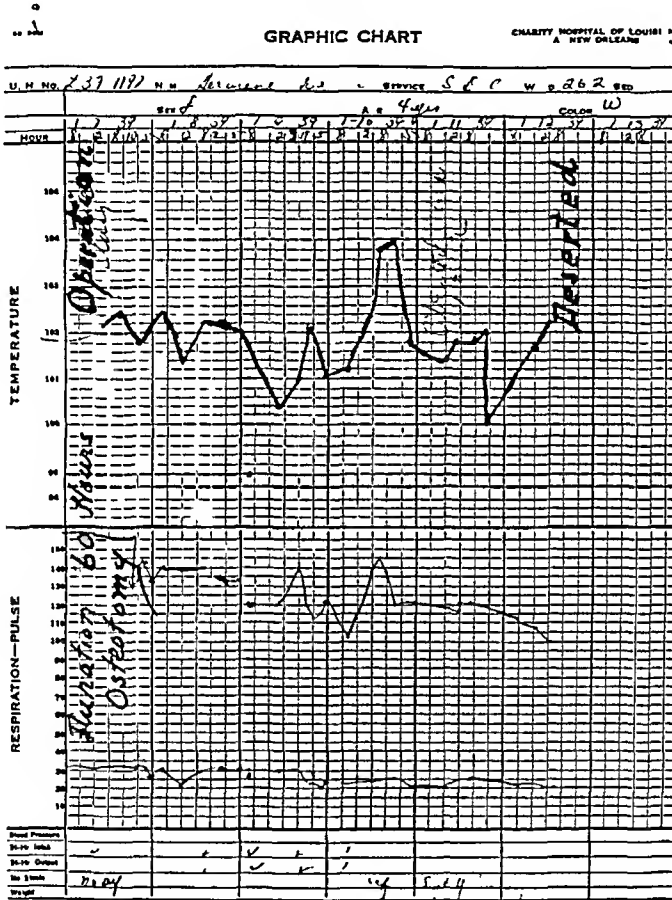


CHART 2—The temperature chart of a child age four years who had an osteotomy performed 60 hours after the onset of the disease. There was no decided drop in the temperature nor subsidence of the systemic evidence of sepsis. The febrile course of acute hematogenous osteomyelitis may be prolonged with or without operation.

and others, have reported encouraging results clinically. The only disadvantage which might be an objection for its use is reactions. These are not common. A reaction was encountered once in this study of the six cases in which antitoxin was employed.

(5) Operation—At the present time, one of the most controversial of all measures for acute hematogenous osteomyelitis, in the primary state, is the status of the value of operation. Our studies show that, in the first series, operation apparently did more harm than good. Certainly, one would not expect a greater mortality rate than 24 per cent if operation had been with-

held. Again, withholding operation, surprisingly, does not result in an extremely high mortality. It would seem that the reduced incident of operation, in the second series, had a great deal to do with the improved mortality statistics. On the other hand, of four deaths which occurred, operation was entirely withheld in two, in one even though the case was seen on the second day of the disease, and of the two remaining deaths, operation consisted merely in draining the abscess. Of the ten cases in the group in which no operation

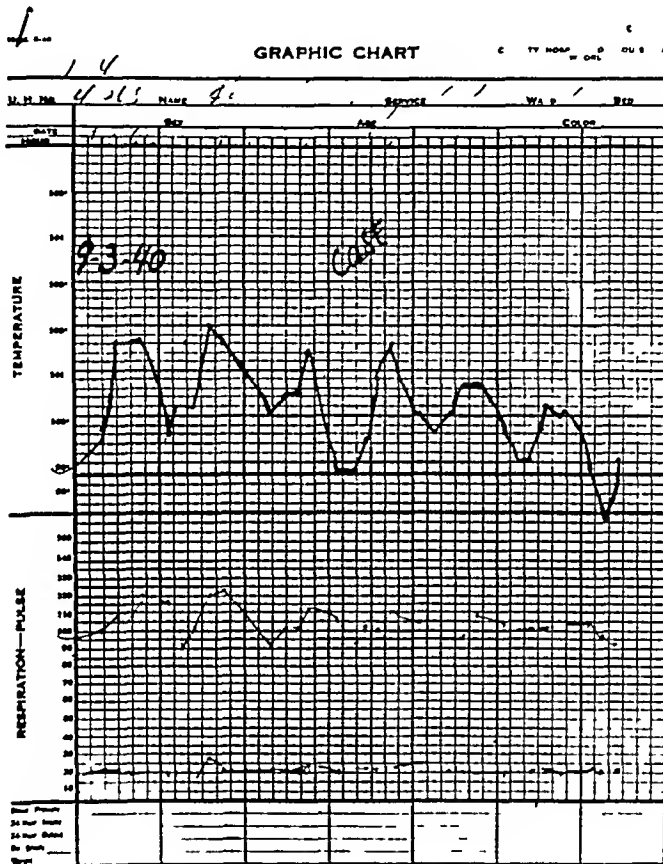


Chart 3A

CHARTS 3 and 3A—The temperature chart of a child age 12 who was admitted on the fourth day of the disease. Incision and drainage of a soft tissue abscess resulted in slight abatement of fever. The subsequent application of a plaster encasement resulted in further improvement. The febrile course was prolonged. The patient was well in eight months.

was performed, death occurred in two. Certainly, these facts would make one wonder whether opening the bone in these cases would not have produced a more desired effect. Because of the numerous factors which come into the study of the improved mortality, it is difficult to evaluate clearly the changes which have gone on in the use or restraint of one therapeutic measure such as operation. We do not wish to draw any inflexible or iron-bound conclusion regarding operation, but believe that adequate drainage, whether by incision of soft tissues only, or by osteotomy, is indicated after the disease had endured long enough for pus to be expected (at least several

days) Disregard of this rule may result in serious mistakes by converting a case which is not osteomyelitis into one which is. Preparation enduring, at least, hours is essential before every operation. Operation is never so urgent that this principle should be neglected. Emergency operation, in the sense that a patient should be immediately taken to the operating room after admission and the bone drilled, carries a prohibitive mortality. Operation, whether incision or osteotomy, should insure adequate continued drainage, preferably by packing with vaselined gauze¹⁴. Vein ligation is indicated in cases with persistent positive blood cultures.

(6) Immobilization—One of the most dramatic of all therapeutic measures is immobilization of an affected extremity. In a number of records where we have carefully checked the temperature charts, we found that the fever would be sustained in spite of operation, administration of chemotherapy and other measures, but, immediately, when the patient was put in a plaster encasement, without any other factor apparently being responsible, the temperature would decline sharply (Charts 3A and 4). Encasements were applied in the acute phase in the majority of these 66 cases. Never, as far as could be seen in studying the record, did the application of an encasement result unfavorably. This is one measure which always should be employed. It may be viewed with skepticism, but to any one who has had experience in absolute immobilization in acute hematogenous osteomyelitis, its value would not be questioned. Immobilization may be by an encasement or traction to affect the involved extremity.

(7) Late Operation—Sequestra sometimes appear in the roentgenograms during the fourth week. Apparently, the removal of sequestra or infected bone may result in a more rapid healing than occurs if the patient is left indefinitely alone. The indications for secondary operations or operations in the third stage of the disease are the appearance of a definite sequestrum in the roentgenogram, only with, however, a continuation of the drainage and inflammatory reaction. Another indication for intervention would be the continual drainage of a sinus in spite of no definite roentgenographic evidence of a sequestrum.

Unfortunately, we saw no evidence in this study that the morbidity of the disease is decreasing. Cases mentioned here have been repeatedly admitted to the hospital eight or ten times over a period of a few years. One had as many as six bone operations, and the disease was still active. This is nothing new in the morbidity of the disease. It is well known but not as well acknowledged. Possibly the developments in immunotherapy and chemotherapy combined with operative procedures will solve the prolonged disability in many of these cases.

SUMMARY AND CONCLUSIONS

The details of the study of 66 cases of primary acute hematogenous osteomyelitis admitted to Charity Hospital, New Orleans, between 1937 and 1940, inclusive, are given, and are compared with a previous study of 112

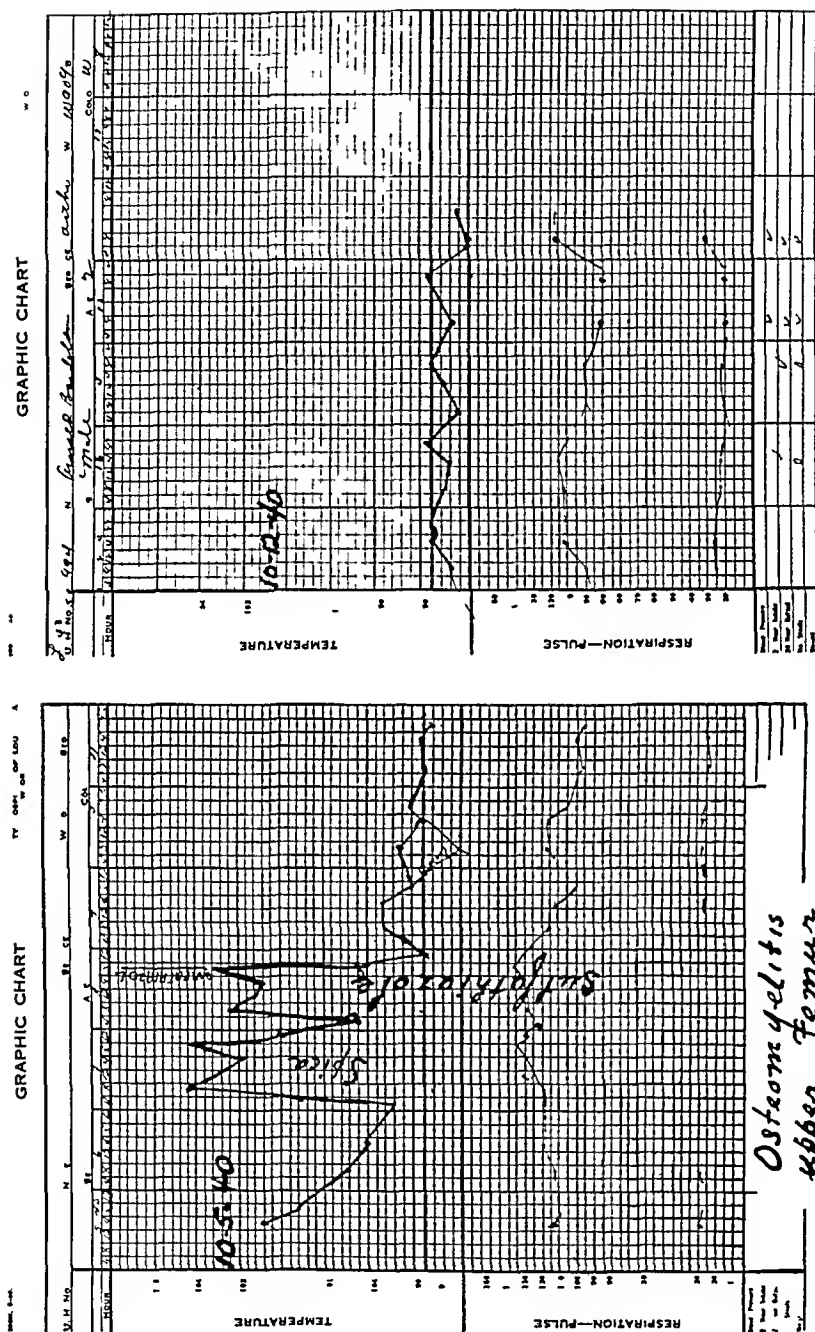


CHART 4.—Temperature chart of a child, age two months, with osteomyelitis of the upper end of the femur. The application of a spice and the administration of sulfathiazole resulted in prompt arrest of the disease although osseous involvement was proved roentgenologically. No operation was performed.

cases occurring at the same institution from 1930 to 1936, inclusive. In the present group of 66 cases, the mortality was 66 per cent, in sharp contrast to a mortality of 24 per cent for the previous group. Efforts were made to disclose the variations in the methods of management which were responsible for the great improvement in the mortality.

Among the most important features responsible for the higher mortality were: Unjustified emergency operation before the patient had been properly prepared, and failure to reestablish normal physiology by fluid and electrolyte replacement and blood transfusions before operations were undertaken. In addition to these factors, new chemotherapeutic measures and immunotherapy have undoubtedly added additional favorable influence in the therapy of the disease. Our study shows, in comparing the two groups of cases, that operation itself performed after preparation is not a deleterious factor, and that opening the bone after essential preparation is no more harmful than incision and drainage.

Evacuation of pus, whether it be by simple incision or by osteotomy, would seem to be a favorable measure in the management of the disease. Osteotomy apparently does not influence the extent of bone involvement. An additional measure of extreme importance, from the operative viewpoint, is vein ligation in cases that have a continuous positive blood culture. Immobilization in a plaster encasement is a measure of great value and of far greater importance than is usually realized. It deserves wider application.

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DISCUSSION—DR MIMS GAGE (New Orleans, La) I have enjoyed Doctor Mahorner's paper very much and think it quite timely, due to our activity in the present emergency. However, traumatic wounds, with fracture, resulting in osteomyelitis, differ etiologically from the juvenile type, but the principles of treatment are quite similar.

I have been interested in acute hematogenous osteomyelitis for many years, and in teaching students have varied somewhat from the accepted classification of the disease. In the past, as well as at present, the majority of surgeons class osteomyelitis as a single diseased state of the osseous system and have treated all cases as such. I believe that this has been mainly responsible for the present and widespread misunderstanding of the disease and, in a way, responsible for the high mortality. There has been very little effort made to distinguish, both clinically and by laboratory methods, the differences that exist in the various types of acute osteomyelitis.

We have many types of osteomyelitis, namely (1) Acute osteomyelitis, with pronounced systemic manifestations due to toxemia and bacteremia (local reaction is not a part of the clinical picture), (2) profound systemic reaction (overwhelming toxemia without bacteremia), with minimal or absent local manifestations, (3) acute osteomyelitis, with quite severe local manifestations, with moderate systemic toxemia without bacteremia, (4) moderate to severe local manifestations, with mild systemic reactions, (5) minimal local and systemic reactions (Brodie's abscess), (6) minor local reactions, with benign systemic reactions (Garie's sclerosing type), and (7) the chronic form. In the past, and at present, these various groups are classed as acute osteomyelitis (except probably No. 6), and treated as such. One school advocates immediate operation, another, conservative treatment for a few days followed by operation, and the third school nonoperative intervention, relying on the "sulfa-cure-all" drugs (sulfonamide group). I am convinced that the above conception (one disease) and the treatment advocated are, to a great extent, responsible for the appalling mortality.

As the *Staphylococcus aureus* is responsible for the greater number of cases (83 per cent), I think we should have some definite knowledge regarding the types and toxins produced by this formidable pyogenic organism. Spink* has isolated over 60 strains of staphylococci from patients, from both lesions and blood stream. We certainly should have some idea with regard to the various toxins liberated by the growth of the staphylococcus. The outline of Spink is quite interesting, and gives us a better insight into both the local pathology and the systemic reactions of acute staphylococcus osteomyelitis.

Spink names the following toxins: Hemolysis, dermonecrotxin, lethal toxin, leucocidin, coagulase, fibrinolysin, enterotoxin, and the spreading factor of Duran-Reynolds.

The lethal toxin factor is of great importance because it can produce death within 15 to 34 hours. The other toxins are responsible for the variation in both the local pathology and the systemic reactions. Therefore, as stated previously, one cannot treat acute osteomyelitis as a single pathologic

* Spink, W W The Pathogenesis and Treatment of Staphylococcal Infections Internat Clinics, 4, 236, 1941

process with one reaction. It must be evaluated from the outline given above, *i e*, the seven different clinical forms. The treatment should be based upon a thorough knowledge of both the local and systemic reactions. In those of profound toxemia and bacteremia, or in those with profound toxemia without bacteremia, and in those with moderate toxemia with bacteremia, immediate neutralization of the toxemia and suppression of bacteremia must be accomplished. In those cases that respond to neutralization of the toxemia but the bacteremia persists, methods must be instituted to delete the bacteremia. Therefore, in these cases staphylococcic antitoxin, in large doses combined with sulfathiazole and immobilization, should be given immediately, with immobilization of the involved limb. If the toxemia subsides and bacteremia persists, ligation of the common femoral vein of the lower extremity and axillary vein of the upper extremity is done, and sulfathiazole medication is continued.

Early operation is definitely contraindicated in the above type of case. Sustaining therapy must also be given. Infusions to maintain water balance and transfusions of whole blood and plasma, to replace and supplement corpuscular and protein loss, are given. Types 3, 4, and 5 should receive chemotherapy, sustaining therapy, early operation and immobilization. Plaster encasements for immobilization can be used safely in these cases. Types 6 and 7 are treated as elective cases. There is no definite indication for emergency treatment in the latter two types. I believe Butler's* report is of great significance as regards the surgical treatment in the acute phase. He reported 123 cases with bacteremia (positive blood cultures), with a mortality of 52 per cent, whereas in 122 cases without bacteremia (negative blood culture) the mortality was only 2 per cent. These mortalities represent those cases in which early operation was undertaken. I think we should ponder at great length on these figures. They demonstrate in a definite manner that which I have tried to point out in my discussion.

It is evident that we must have a thorough knowledge of all the factors involved, etiology, type of organism, type of toxin liberated, the systemic effect of the toxin on the organism, the local pathologic process, and its mode of extension, and the surgical principles involved, before we can intelligently treat cases of acute osteomyelitis and reduce the present high mortality and morbidity.

I wish to condemn the extensive habit and practice of "selling-short" sound, surgical principles, based upon pathologic physiology, for a limited supply of the "sulfa-cure-all" group of drugs, for indiscriminate application and use.

DR JOSEPH E J KING (New York, N Y) I should like to ask Doctor Mahoney two questions. First, has the use of sulfathiazole helped in the prevention of massive destruction of the skull in cases of osteomyelitis, and second, has it been of any value in the treatment of osteomyelitis of the vertebrae? We have had a number of cases in which massive resection of the skull has been done in the past, before the day of chemotherapy. In these cases, regardless of the type of infection in the accessory nasal sinuses, the infection in the skull is usually due to *Staphylococcus aureus*. In view of the fact that Doctor Mahoney's cases have been so successfully treated with the use of the sulfonamide drugs, it is possible that the massive resections of the skull formerly undertaken may be eliminated.

* Butler, E C. The Treatment, Complications and Late Results of Acute Hematogenous Osteomyelitis Based on a Study of 500 Cases Admitted to the London Hospital, During the Years 1919-1937. Brit Jour Surg, 28, 261, 1940-1941.

DR L. D. BAKER (Durham, N. C.) I want to thank Doctor Venable for his remarks in regard to the work at Duke Hospital on staphylococcal infection, and for inviting me to discuss this paper.

The therapy Doctor Mahorner has outlined is essentially the same as we try to carry out at Duke Hospital. There is no disease which requires more acute surgical judgment or which has a wider range of severity than hematogenous osteomyelitis. In analyzing end-result studies, the cases should be grouped under several headings if the conclusions are to be of value. In conducting our studies we have classified hemolytic *Staphylococcus aureus* osteomyelitis under four headings: (1) Localized osteomyelitis without blood stream infections, (2) localized osteomyelitis with transitory bacteremia, (3) osteomyelitis with metastases and bacteremia but without toxemia, and (4) osteomyelitis with bacteremia and toxemia. It is the latter group that are, as a rule, so severely ill, and in outlining their therapy one must keep in mind the four actions of staphylococcus toxins, namely, (a) the hemolysis of red blood cells, (b) the destruction of young leukocytes, (c) the coagulation of plasma, and (d) the necrosis of tissue.

If a patient is unable to manufacture sufficient amounts of antitoxin, we feel that commercial antitoxin, as prepared by the Lederle Laboratories, is of inestimable value in either neutralizing or counteracting the actions of the staphylococcus toxins. When toxemia is present the patient is having his natural defenses destroyed, in that the polymorphonuclear cells are prevented from reaching maturity. In addition there is a hemolysis of the red cells, a coagulation of the blood plasma, resulting in thrombosis of the vessels about the area of infection, and a necrosis of tissues. Occasionally a patient is capable of neutralizing the hemolyzing toxin and the leukocyte-destroying toxin, but at the same time he may be sensitive to the breakdown products of his own tissues. Like Doctor Mahorner, we believe that after proper preoperative steps have been taken, incision and drainage is indicated in the majority of cases. In addition to general supportive measures the use of staphylococcal antitoxin when indicated, surgery at the proper time, and as it appears that sulfathiazole is of benefit in this type of infection, its use is indicated as an adjunct in the therapy. The same cannot be said of sulfanilamide and sulfapyridine, in fact, in our hands, because of the toxic action on the vascular system of the two last-named drugs, we think they are contraindicated in the presence of a hemolytic *Staphylococcus aureus* infection.

DR HOWARD MAHORNER (New Orleans, La., closing) If there is any one thing this sort of study shows, it is that the old doctrine, that the one important measure in treatment is operation, is a fallacy. The first slide (Fig. 7) with the tremendous mortality (24 per cent) showed that operation alone does not save lives. The improvement we have had is not because we withheld operation, but because the patients were better prepared. Patients with septicemia should be treated with modern physiochemical measures. There is no question about that, but there is some question about the time of operation in these cases.

How can one prove the value of operation? It is still an open question. No one could present better figures than Penberthy and Weller, who reported 19 cases in which they performed immediate operation with no mortality and relatively low morbidity. This looks as though operation were an important factor in therapy, but the same measures with and without operation may give a very small difference in mortality. This has to be studied from every angle. Most important is preparation for operation by replacement of fluids and electrolytes, blood transfusions, and chemotherapy.

Doctor Baker and Doctor Shands have shown immunotherapy to be of value in this condition. After preparation, adequate drainage is indicated, and in certain cases vein ligation is indicated. Immobilization in a plaster encasement is one of the most important measures. The late stage operation was not even considered in this study, because it is a question of improving the prolonged morbidity. That is going to be more difficult than reducing the mortality in the acute phase.

In reply to Doctor King's question. We have not had enough cases treated with chemotherapy to know whether we have had fewer metastatic lesions. The percentage of patients with multiple foci was just as high in this recent series.

SPLENECTOMY *

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THE REMOVAL of certain important organs of the body as a therapeutic measure comprises a large part of the surgeon's pharmacopoeia. The spleen is one of these organs. The reasons for its removal are not quite clear but by a trial and error practice it has been found that the removal of the spleen in certain instances results in the disappearance of dangerous symptoms. We do not like to acknowledge the fact that the reasons for the improvement and cure of these conditions following splenectomy are not understood. Until the cause of these diseases is understood we will continue to perform splenectomy for certain groups of symptoms.

The accumulation of results of many splenectomies has resulted in definite indication for the operation in certain diseases and equally definite contraindications in other diseases associated with enlargement of the spleen.

Experience has shown that splenectomy is not indicated where splenomegalia is of septic origin or in myelogenous leukemia, pernicious anemia, lymphoblastoma and polycythemia vera, syphilis and malaria. On the other hand, there is no longer any doubt of the advisability of splenectomy in other diseases. These are purpura hemorrhagica, hemolytic icterus and less surely splenic anemia or Banti's disease. The results of splenectomy in the first two conditions are almost specific with few failures if the patient survives the operation. In Banti's disease good results may be expected early in the disease but late in the disease after there is great liver damage and ascites, in our own experience, the improvement is only temporary. Soon partial obstruction and repeated hemorrhages from *esophageal varices* prove fatal.

In young individuals there is difficulty in classifying many splenomegalia cases under one of the above named diseases. Splenectomy in such cases, if it can be undertaken with safety, may often be advisable. It is not our intention here to review the well known theories of diseases of the spleen, but to discuss operative procedures for reducing the mortality in splenectomy.

First, the preparation of the patient and selecting the proper time for the operation is of great importance. In the more advanced cases liver damage has already occurred and reinforced glucose feedings are not to be overlooked, while in severe anemia and particularly in purpura hemorrhagica (thrombocytopenia) transfusions and carefully watching for a favorable time for operation will save the severe cases.

Hemorrhage, both operative and postoperative, should be guarded against. The use of an incision which gives adequate exposure and at the same time is anatomically placed, so that a sound abdominal wall will be assured, has made us feel more confident of a successful outcome. The operation, which has been previously described,¹ is as follows. "The patient is tilted slightly to the

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941

right side The skin incision is begun in the midpigastrie line, half way between the ensiform and umbilicus, and is extended laterally and downward to just above the crest of the ilium, which is in the line of the fibers of the internal oblique muscles The anterior sheath of the rectus muscle is incised and the incision is carried across the fibers of the external oblique fascia to where it becomes muscular The rectus sheath is dissected off its muscle upward and downward for a short distance and the muscle is retracted medially This exposes the posterior sheath which is incised across from the linea alba outward and downward and between the fibers of the internal oblique The transverse muscle is cut in the same line without separating it from the internal oblique The tenth intercostal nerve is retracted with the rectus muscle, while the eleventh nerve is cut and the twelfth is retracted laterally



FIG 1—Incision parallel to costal border from midline to just above anterior superior spine

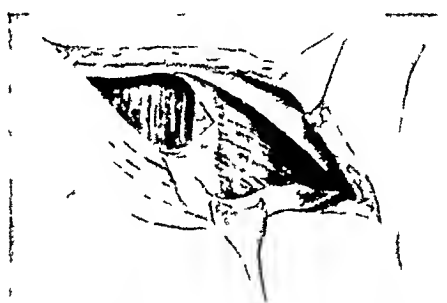


FIG 2—Anterior sheath of rectus and fascia of external oblique incised

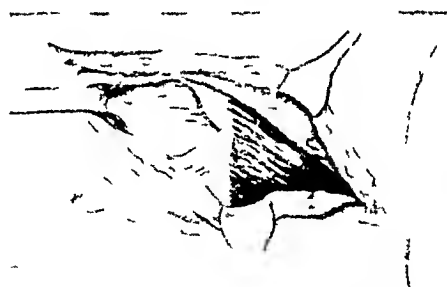


FIG 3—Anterior sheath dissected free of rectus and rectus retracted medially

"The use of a gastric suction tube put in place before the anesthetic is started, to collapse the stomach, gives greater room, and if it is retained for 24 to 48 hours it lessens the danger of displacing ligatures off the greater curvature of the stomach and also results in a smoother convalescence

"The ligation of the splenic artery may not be visible, but its pulsation will be felt along the upper border of the pancreas when the lesser peritoneal cavity is opened Care should be taken not to tear or include the splenic vein in the ligature Almost immediately the spleen will reduce in size, thus making the gastrosplenic vessels accessible for severing between ligatures placed well away from the stomach The separation of the spleen from the splenic flexure of the colon and upper pole of the kidney is next done, with careful ligation of all structures severed Only now should the spleen be delivered out of the abdomen After the spleen has been freed of its attachment to the diaphragm,

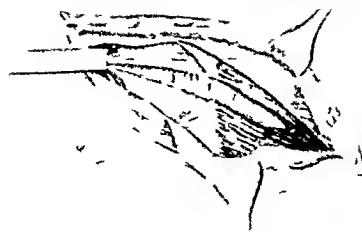


FIG 4—Posterior sheath of rectus and peritoneum incised and continued between fibers of the internal oblique and across transversus muscle



FIG 5—Lesser peritoneal cavity entered and splenic artery (along upper border of pancreas) ligated



FIG 6—Gastro-splenic omentum is divided between ligatures all the way to the diaphragm. Also spleno-colic ligament is divided

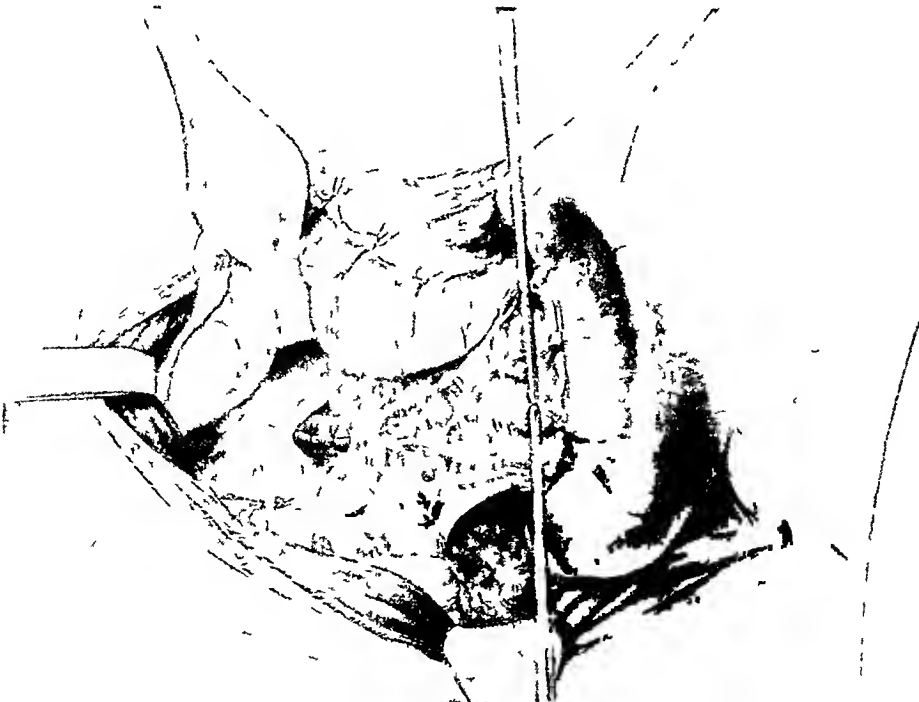


FIG 7—The spleen is then delivered out of the abdomen, the remaining pedicle divided and ligated

the remaining hilus structures are clamped and then ligated. Following removal of the spleen, there is good exposure of the diaphragm and oozing vessels may be clamped and tied or coagulated with the radiocautery. Thus a dry bed is left and the necessity of packing with gauze is obviated. A continuous stitch sutures the posterior rectus sheath and the transverse and internal oblique muscles with the peritoneum. A second suture closes the anterior rectus sheath and external oblique fascia. A strong abdominal wall results.

"The incision is unanatomic in that the fascia of the external oblique, as well as of the transverse muscle, is cut across its fibers. The injury to the intercostal nerve leaves no permanent evidence of damage, either to sensation or muscle control."

A review of a fairly large series of splenectomies shows a mortality of 9 to 30 per cent. In general hospitals where there is a large number of advanced cases requiring splenectomy the mortality is very high. These patients are bad risks and a certain mortality is unavoidable. On the other hand, deaths not infrequently result from hemorrhage incident to the operation from the tearing of vessels or the accumulation of blood intra-abdominally from oozing of blood from the splenic bed. In a series of 30 splenectomies with five deaths, at autopsy, there were found in three cases intra-abdominal accumulations of blood in excessive amounts which might have been avoided with a better exposure of the diaphragm and direct attention to capillary bleeding.



FIG 8—The posterior sheath of the rectus, internal oblique transversus and peritoneum closed in one layer



FIG 9—The anterior rectus sheath and external oblique fascia is closed with a second layer

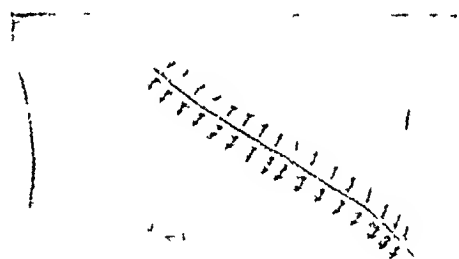


FIG 10—Skin incision closed

REFERENCE

- ¹ Singleton, A. O. Splenectomy. Surg., Gynec., and Obstet., 70, 1051-1053, June, 1940.

DISCUSSION—DR. J. D. RIVES (New Orleans, La.) I would like to express my appreciation of Doctor Singleton's very interesting demonstration of his careful anatomic technic of splenectomy. I would also like to comment on one problem upon which he did not touch, that is, the mobilization of the spleen in the presence of very extensive and dense adhesions that cannot be separately divided and ligated. In some instances, the peritoneal covering of the spleen may be completely fused with the parietal peritoneum covering the diaphragm and the lateral abdominal wall. I have found that under such circumstances an attempt to separate the spleen from the parietal wall usually

results in deep laceration of the spleen, which is followed by violent hemorrhage. This hemorrhage is chiefly from the spleen itself rather than from the adhesions. I have found that under such circumstances if an incision is made through the parietal peritoneum anterior to the attachment of the adhesions, the loose areolar tissue underlying the parietal peritoneum provides a line of cleavage in a relatively avascular plane. The hand may be inserted into this plane and, by rapid blunt dissection, the entire spleen may be mobilized with great ease and a minimum of hemorrhage.

When the spleen is delivered it is covered by a double layer of peritoneum, that is, both the parietal and the visceral layers. The remainder of the procedure is then carried out in the conventional manner. This maneuver exposes the posterior surface of the lienorenal ligament uncovered by the peritoneum, and the identification of the structures of the pedicle, including the tail of the pancreas, is comparatively easy. A large raw surface is left behind but this may be readily covered by omentum if desired. It is probable that the greater curvature of the stomach would become adherent if this were not done but it is doubtful whether or not this would interfere seriously with the function of the stomach. This method is not frequently needed, but it has saved me very serious difficulties on two occasions.

DR R. L. SANDERS (Memphis, Tenn.) Doctor Singleton has been a champion of the transverse incision for many years, and it was largely because of his successes that I became interested in this approach to the upper abdomen.

My experience with the transverse incision has been confined chiefly to operations on the gallbladder and ducts, perforated peptic ulcer, and congenital pyloric stenosis in infants. For splenectomy, the transverse incision on the left has been found most satisfactory. We have now applied the various types of approach in approximately 600 cases. In our early cases, the incision was made across the linea alba, with this technic, however, a few infections developed, followed by separation of the wound and hernia. Later, we adopted the method suggested by Doctor Schwyzer, of St. Paul, and this incision of Doctor Singleton's, and, so far as we know, none of the patients has had a hernia. The incision is admirably suited to the Ramstedt operation for pyloric stenosis. Disrupted wounds in crying babies are sometimes fatal in these cases. Practically all such deaths occur following the employment of the vertical incision. When the incision is transverse, crying tends to draw together, rather than separate the wound edges, and thus there is little danger of wound disruption.

The transverse incision is also especially advantageous in operations upon obese individuals beyond middle age, whose abdominal walls are composed chiefly of fat and thinned-out muscles and fascia. As these patients generally take the anesthetic poorly, respiratory effort is increased and closure of the vertical incision is difficult. This difficulty is obviated by the use of the transverse approach.

Unquestionably, the transverse incision has a definite place among surgical approaches, and once the technic is mastered, its advantages are readily appreciated.

THE USE OF ESTROGENIC SUBSTANCES IN THE PRE- AND POSTOPERATIVE TREATMENT OF HYPERTHYROIDISM*

FURTHER OBSERVATIONS

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DURING the meeting of the Southern Surgical Association, in 1940, at Hot Springs, Va., one of us (A. H. S.¹) discussed the use of estrogens in conjunction with the surgical treatment of hyperthyroidism. The results observed in a small series of cases in which this supplementary medication was employed, have been reported,² along with a review of the rationale for the employment of this form of therapy. The present report includes additional recent observations which confirm the previous findings.

Observations upon which the employment of estrogen therapy in hyperthyroidism is based include those by Sherwood and Bowers,³ and Sherwood,⁴⁻⁷ which demonstrated the basal metabolism lowering effect of estrogens in thyroidectomized animals rendered hyperthyroid by the feeding of thyroid substance, the observations by Starr and Patton,⁸ that an increased sensitivity to thyrotropin exists in hyperthyroidism, the thyroid stimulating effect of thyrotropin,⁹⁻²¹ and the direct metabolism stimulating effect of certain anterior pituitary secretions.²²⁻²⁹ The exact mechanism of basal metabolism lowering observed in hyperthyroidism is not agreed upon. Sherwood and Bowers,³ and Grumbrecht and Loesei³⁰ advanced the hypothesis that the basal metabolism lowering effect is mediated through an inhibitory influence exerted by the estrogenic substances on the anterior pituitary. Later observations by Sherwood,^{6, 7} however, led him to believe that the basal metabolism lowering effect of estrogenic substances is due to a direct hormone antagonism in the tissues rather than to an influence on the thyroid gland either directly or by mediation through the pituitary gland. In addition to any possible effect which retardation of anterior pituitary thyrotropic hormone secretion might have in reducing thyroid activity, inhibition of the direct tissue metabolism stimulating effect of anterior pituitary secretions²²⁻²⁹ might at least partially account for any lowering of the metabolic rate following the administration of estrogenic substances to patients with hyperthyroidism.

Eleven cases, including five previously reported,¹ constitute the basis for the present report. As controls, 11 cases of surgically treated hyperthyroidism, which received practically the same basic preoperative therapy as did the cases which were treated with estrogens, were studied.

The race, sex, and age factors in the control and estrogen treated groups are shown in Chart I, which also shows the incidence of iodine-fast cases in the two groups. Average age was considerably greater in the control group.

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941.

The cases which received estrogen therapy presented clinical evidence of greater toxicity (nervousness, tremor, apprehension, palpitation, purposeless movements) than did most of the cases in the control group. This clinical impression of greater toxicity in the group selected for estrogen therapy was confirmed by the slightly higher average basal metabolic rate on admission,

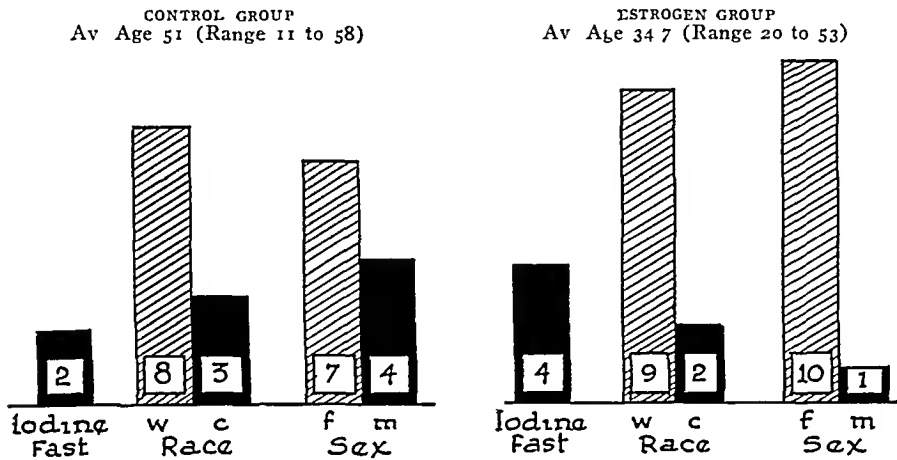


CHART 1—Showing age, incidence of iodine fastness, race and sex in control and estrogen treated cases

+47.7 per cent, as shown in Chart 2 and a higher average pulse rate, 113 beats per minute (Graph 1), than in the control group, in which these values were +46.9 per cent, and 109, respectively. Three cases of the estrogen treated group and four of the control group had nodular toxic goiters. The remaining cases in both groups had diffuse toxic goiters. Of the 11 cases

Comparative lowering to B. M. R. in response to basic treatment

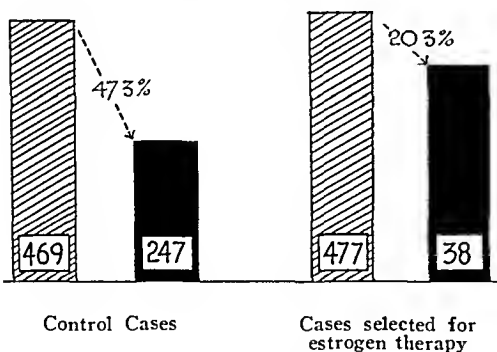


CHART 2—Showing average basal metabolic rate on admission and following 'basic' therapy in control group and group selected for estrogen therapy

which received estrogen therapy, four were estimated to be sufficiently toxic to require two-stage operations, whereas two-stage operations were performed in only three of the 11 cases in the control group. In the instance of cases in which multiple-stage operations were performed, only those observations which were made preceding, during, and immediately following the first stage are included in the data presented. Four of the 11 estrogen treated cases had received iodine elsewhere for periods varying from four to eight months prior to

hospital admission. Of the control group, one case received iodogeno-therapy and another case received Lugol's solution before hospital admission. All one-stage operations consisted of subtotal thyroidectomy, and in multiple-stage operations, one lateral lobe or a lateral lobe and the pyramidal lobe were removed at the first operation. Estrogen therapy was continued following

operation when only one lobe was removed at the first operation. There were no deaths in the estrogen treated cases, one patient in the control group, having a basal metabolic rate of +81 per cent on admission, died following a one-stage subtotal thyroidectomy.

In both the control and the estrogen treated groups, the basic preoperative preparation included bed rest, sedation by means of sodium bromide, a high caloric diet, calcium gluconate grains 15 t i d, large doses of vitamins A, B₁ or B complex, C, and D, as well as Lugol's solution minims 10-15 t i d. In one of the estrogen treated cases iodine administration was delayed until not later than six days preoperatively, while in other cases of the estrogen treated group institution of iodine therapy antedated the administration of estrogenic substances.

TABLE I

SUMMARY OF DOSES OF ESTROGEN

Showing variations in type of estrogen used dosage and response as shown by pulse and basal metabolic rates on admission after basic therapy and preoperatively following estrogen administration

Case No	Total Dose	Dose Schedule	Response	
			a—on admission, b—after basic therapy, c—following estrogen	B M R
1	12,000 u theelin	2 000 u daily for 6 days preceding operation	a—125	a—81
			b—120	b—47
			c—105	c—46
2	100 000 u theelin	10 000 u daily on 12 days preceding operation (2 days omitted)	a—110	a—27
			b—110	b—29
			c—110	c—25
3	10 000 u theelin	One dose on day preceding operation	a—135	a—73
			b—120	b—42
			c—90	c—35
4	20 000 u theelin 4 mg diethylstilbestrol	10 000 u daily on 2 days preceding operation 24 hours preoperatively	a—110	a—78
			b—115	b—58
			c—127	c—55
5	30,000 u theelin	10 000 u daily for 3 days preceding operation	a—107	a—37
			b—115	
			c—90	c—8
6	60 000 u theelin 16 mg diethylstilbestrol	10 000 u daily on 15th 16th 17th 18th 19th 20th day prior to operation 4 mg t i d on 7th 8th 9th 10th day prior to operation	a—90	a—24
			b—82	
			c—85	c—30
7	250 mg diethylstilbestrol	Given during the 15 days preceding operation	a—110	a—33
			b—115	b—33
			c—90	c—25
8	218 mg diethylstilbestrol	Given during 30 days prior to operation	a—90	a—60
			b—100	b—60
			c—85	c—30
9	4 mg diethylstilbestrol	1 mg daily for 4 days prior to operation	a—140	a—58
			b—115	b—48
			c—95	c—44
10	20 000 u theelin 56 mg diethylstilbestrol	10 000 u on each of 8th and 9th days prior to operation Given during the 9 days preceding operation	a—105	a—31
			b—105	b—31
			c—105	c—11
11	242 mg diethylstilbestrol	Given during 30 days preceding operation	a—110	a—33
			b—130	b—45
			c—90	c—27

The estrogens employed were either theelin in oil, administered intramuscularly, or diethylstilbestrol, administered orally. In several instances both of these preparations were employed in the same case.

All of the estrogen treated cases received intravenous pentothal sodium anesthesia immediately before being brought to the operating room. Three of the control group received pentothal sodium intravenously, and one received tribromethanol per rectum as a means of inducing basal narcosis. Ethylene and oxygen supplemented with ether were administered to five control cases and eight estrogen treated cases. Ethylene and oxygen was given to four of the control group. One of the control group received nitrous oxide and oxygen and one received cyclopropane and oxygen. Three of the estrogen treated group received cyclopropane and oxygen at the time of operation.

The dose schedule, as well as the total amount and type of estrogenic substance employed, varied considerably (Table I). The table also indicates the responses of the individual cases. It is noteworthy that only one case, after receiving 56 mg. of diethylstilbestrol, was nauseated and complained of itching. On account of the uncertainty of the effects of estrogens in hyperthyroid patients, small doses were first used. Later, larger doses were employed and three cases received over 200 mg. of diethylstilbestrol by mouth. The possibility of refractoriness following repeated doses of estrogens has been discussed in a previous report.²

A comparison of the average changes in basal metabolic rates in response to basic treatment in the estrogen treated group, with the corresponding changes which occurred in the control group, is shown in Chart 2. An additional 10.9 per cent average lowering of basal metabolic rate in this group followed estrogen therapy (Chart 3).

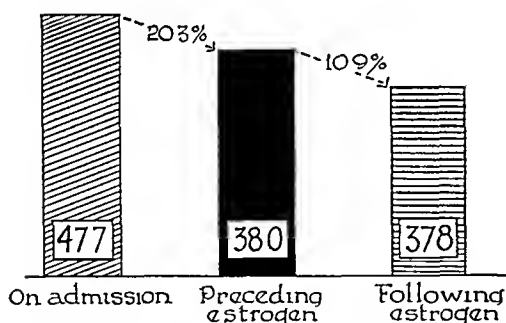


CHART 3—Showing the additional lowering in basal metabolic rate which followed estrogen therapy in the group of cases which had shown refractoriness to basic treatment.

Comparison of the average changes in pulse rates, in response to treatment and operation, are shown in Graph 1. Following estrogen administration the average pulse rate reached a level as low as that attained in the control group. Although the peak pulse rate during operation in the initially more toxic group which received estrogen therapy was slightly higher than that of the control group, the lower average peak pulse rate on the first post-

operative day in the estrogen treated cases is significant, and is in accord with the better subjective feeling and the general appearance at that time, of the estrogen treated patients. This observation is of particular significance because of the greater number of patients in this group who had one thyroid lobe still functioning after operation. Preoperative preparation in the control and estrogen treated groups averaged 25.6 days and 14.7 days, respectively.

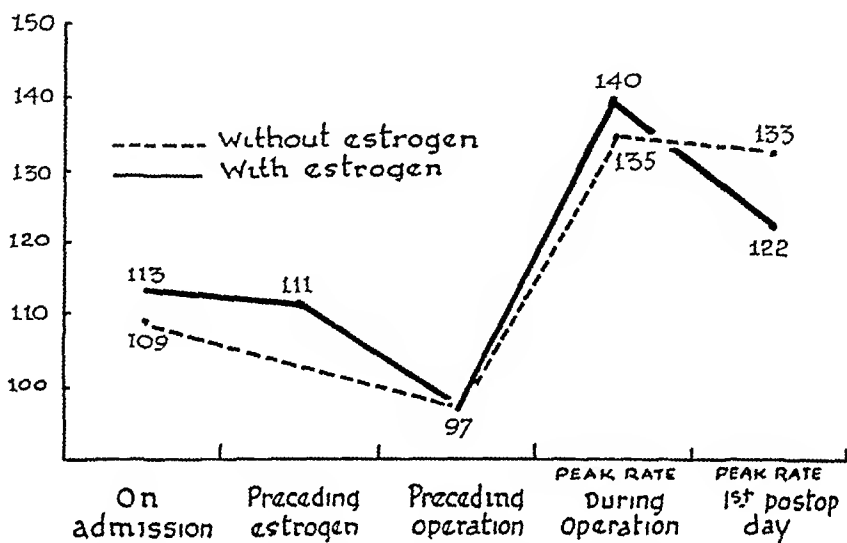
SUMMARY AND CONCLUSIONS

(1) The rationale for the employment of estrogen therapy in hyperthyroidism is discussed.

(2) Therapy with estrogenic substances was employed in 11 cases with hyperthyroidism having an average basal metabolic rate of $+47.7$ per cent, four of which were iodine-fast and four of which manifested such toxicity as to be considered to require multiple-stage operations

(3) The response to preoperative treatment and operation of the estrogen treated cases is compared with corresponding observations made in 11 cases of hyperthyroidism in which estrogenic therapy was not employed

(4) The patients who received estrogen therapy consistently looked and felt better than did the control group. This difference was most pronounced during the immediate postoperative period



GRAPH 1—Showing comparison of average pulse rates on admission following basic treatment, following estrogen the peak pulse rate during operation, and the peak pulse rate on the first postoperative day

(5) An average preoperative lowering of pulse rate equal to that which occurred in the control group was observed in the estrogen treated cases, even though more of the cases which received estrogen therapy were iodine-fast at the time of admission

(6) The average peak pulse rate of the first postoperative day in the cases which received estrogen therapy was lower than was the average peak pulse rate on the same day in the control group

(7) No crises occurred in the estrogen treated group, and there has been no opportunity to observe the possible effects of estrogen administration in the presence of this complication, but it is suggested that estrogen therapy may be of value both for the prevention and treatment of thyroid crisis, especially following a first-stage lobectomy

(8) Although no definite conclusions can be drawn concerning a relation between dosage and effect comparison of the presently reported observations with those following smaller average doses,¹ suggest that small doses of estrogenic substances are equally as effective as large doses, if not more so. Reference is made to the possibility of refractoriness to estrogen therapy following repeated doses. From observations made so far, it appears that

estrogen therapy is most effective when administered for from four to seven days preceding operation when subtotal thyroidectomy is undertaken in one stage. When multiple-stage thyroidectomy is performed, it seems advisable to continue estrogen therapy for several days following the first stage, and, especially if there is a lapse of more than a week between operations, to reinstitute estrogen therapy preceding the second stage.

(9) The present observations imply that estrogen therapy is valuable only as an adjunct in the surgical treatment of hyperthyroidism. So far, no significant difference has been observed in the response to estrogen therapy by patients with toxic diffuse goiters compared with those with toxic nodular goiters.

(10) The number of cases in which estrogen therapy has been employed is too small for the results to be statistically significant. Individual variations, and variations in the timing and amount of estrogen therapy prohibit extrapolation of the present findings. From the observations so far made and herein reported, it is believed that employment of this form of collateral therapy is warranted, especially in (a) severe cases of hyperthyroidism, and particularly when the severity of the disease is of such degree that multiple-stage procedures are necessary, and (b) in iodine fast cases.

(11) No conclusions can be drawn concerning the relative values of theelin and diethylstilbestrol as estrogenic substances suitable for use in hyperthyroidism.

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DISCUSSION—DR HUGH H TROUT (Roanoke, Va) I have had absolutely no experience with these estrogens, but we have had plenty of experience with bromides in mental cases, which I thought might be interesting

We had two hyperthyroid cases which were mentally upset, with hallucinations and other signs which we thought at first were due to thyrotoxicosis, and we should be on the outlook for bromide retention. I do not know how many of you are familiar with the situation relative to the too free use of bromides. The taking of bromides has become an American habit, so much so that now very few patients are admitted to the State or Veterans' Hospitals for the mentally sick without a study of the blood bromides. It is very interesting that the bromides apparently remain fixed in the blood until released by the administration of normal saline. When this is done the mental symptoms usually disappear rather promptly. That is what happened in these two thyroid cases with mental symptoms until we used intravenous normal saline. In the other, the mental symptoms disappeared before operation after the intravenous use of normal saline. I think it is a very serious condition that our State and Veterans' Hospitals for the mentally sick have so large a proportion of patients who have this history of having taken bromides. It might be advisable for us, as surgeons, to have pre-operative study made of blood bromides in our surgical cases with mental symptoms.

INTESTINAL ANTISEPSIS WITH SULFONAMIDES*

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IN DECEMBER, 1940, a preliminary account of the use of sulfamylguanidine in the preparation of the colon for surgical procedures was given before the Southern Surgical Association.¹ No conclusions were drawn from the 12 case records that were presented. It was emphasized that the report was to be looked upon as an initial step in a far-reaching study. It seemed clear that we had found a new application for chemotherapeutic substances, namely, the elimination of pathogenic bacteria from the alimentary canal before surgical procedures are attempted. Our clinical experiences with sulfamylguanidine grew rapidly, and it soon became apparent that this drug was far from satisfactory. We found that it is often ineffective in the presence of ulcerative lesions, that in many instances the drug has to be given in large amounts at four-hour intervals to bring about a significant reduction in the bacterial count in the stool, and also that sulfamylguanidine has little or no effect upon certain pathogenic bacteria within the bowel. Furthermore, from experimental and clinical studies it was shown that the original claim that sulfamylguanidine is poorly absorbed from the gastro-intestinal tract is incorrect.² The drug is readily absorbed from the small intestine, and the low concentration found in the blood is due to rapid elimination of it by the kidneys. For this reason sulfamylguanidine should not be given to any patient having intestinal obstruction or impaired renal function. These observations, together with a report of the occurrence of mild toxic reactions, were presented in April, 1941, before the American Surgical Association,³ and led us to abandon the use of sulfamylguanidine and to commence a systematic search for a compound of high antibacterial potency, low toxicity, and poor absorbability from the gastro-intestinal tract. The successful completion of this effort is largely due to the skill of E. J. Poth, who laid the foundation for the experimental work by constructing an apparatus for accurately feeding dogs a fixed amount of drug at regular intervals. We were able to test, simultaneously, many compounds. At least three sulfonamides were found that have the desired properties. One of these, succinyl sulfathiazole,[†] has been extensively studied on experimental animals and on 120 patients.⁴

When succinyl sulfathiazole is given by mouth in adequate amounts, and at proper intervals one notices that the contents of the gastro-intestinal tract are altered. The stools become soft and odorless and the amount of flatus

* Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941.

† As far as the author can find out, succinyl sulfathiazole was first synthesized by Dr. Melvin Moore, of the Sharp and Dohme Laboratories.

is diminished. These changes reflect the alterations that take place in the bacterial flora. We have found that certain organisms are particularly susceptible to succinyl sulfathiazole, whereas others are unaffected by it. In the former group are *B. coli*, *B. dysenteriae* (Shiga, Flexner and Sonne), and in the latter group are *B. typhosus*, *alpha Streptococcus fecalis*, and *B. proteus*. In order for succinyl sulfathiazole to exert an antibacterial effect in the alimentary canal it is necessary for the drug to get into contact with the mucosa.

Ulcerative lesions retard but do not destroy its efficiency. A blind loop which is inaccessible to the drug will prevent a fall in bacterial count in the stool. Similarly, severe constipation or an active diarrhea interferes with the antibacterial action of the drug. The fresh stool of animals which have been given succinyl sulfathiazole for several days will contain from 50 to 200 mg of free sulfathiazole. Upon standing at 37° C the proportion of this compound to succinyl sulfathiazole rises rapidly, thus indicating that the latter is progressively hydrolyzed to form free sulfathiazole.

We have given succinyl sulfathiazole to more than 120 patients in the Johns Hopkins Hospital and the Union Memorial Hospital, in Baltimore. As judged by changes in the number of coliform bacteria in the stool, it can be said that in almost every instance the ingestion of adequate amounts of this compound lowered the concentration of *B. coli* to less than 1,000 per gram of wet stool. Frequently there were fewer than 100 of these organisms per gram of stool. The only exceptions to these results have been in two patients with blind loops, two with intractable diarrhea, and one child with chronic intestinal indigestion. In two patients having large ulcerated carcinomata of the colon the administration of the drug had to be stopped because of an alarming hemorrhage. In all of the 120 patients succinyl sulfathiazole was poorly absorbed in the alimentary canal, even in those with impending intestinal obstruction. The concentrations of succinyl sulfathiazole and sulfathiazole in the blood of the patients at the Johns Hopkins Hospital were regularly determined and found to average less than 2 mg per cent. The average urinary excretion was 4.85 per cent of the total amount of drug given by mouth. Since this compound has a free carboxyl group, it forms salts easily and, consequently, can be excreted in the urine in high concentration. In none of the patients studied has there been fever, rash, nausea or vomiting attributable to the drug. In all of the patients having large bowel resections there has been primary healing despite the opening of the bowel at the time of the anastomosis.

The usual daily dose of succinyl sulfathiazole is 0.25 Gm per Kg of body weight. It is preferable to give this in six portions, that is, at four-hour intervals. It is important to omit cathartics, especially mineral oil, when using this compound. In patients with severe diarrhea the dose is double the ordinary one. The drug should be given for a period of from 5 to 7 days before operating on the colon and should be continued for 10 days postoperatively when anastomoses have been performed.

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DISCUSSION DR EDGAR J POTH (Baltimore, Md) I should like to take this opportunity to thank you for extending me an invitation to attend this meeting and for the privilege of discussing this paper. Also, I want to express my appreciation to Doctor Firor for his detailed presentation of those phases of this investigation with which I have been concerned.

A study of some 30 sulfonamides with dibasic acid substitutions on the primary para-amino group has uncovered several compounds showing strong bacteriostatic action locally in the bowel. Many of these drugs, however, are highly toxic. Of the substances studied, succinyl sulfathiazole has the best therapeutic ratio. The concentration of any of these compounds in the blood is not necessarily a true index of the toxicity, because the kidney threshold might be low and the drug be rapidly excreted, or the compound might be excreted readily by the liver into the bile to be returned to the gastrointestinal tract. The toxicity of any one drug is probably linked with the total quantity of drug actually disposed of by the tissue cells of the body.

That the chemotherapeutic properties of succinyl sulfathiazole are influenced by the free carboxyl group of the substituting side-chain is indicated by the extent to which the drug is excreted in the bile. An accurate analytic method for the determination of this substance in bile is not available, but crude analytic procedures indicate that considerable quantities of the drug are excreted by the liver. Furthermore, the concentration of the drug and the bacteriostatic response in the feces of animals receiving the compound parenterally show that considerable quantities of the substance are being excreted into the bowel by way of the liver, pancreas, or intestinal mucosa.

The daily intravenous administration to dogs of 2 Gm per Kg of succinyl sulfathiazole causes no gross or microscopic cellular damage. The animals usually vomit once immediately following the injection. Shortly thereafter the animals eat and have no loss of appetite. There is excessive salivation.

In order that the effectiveness of succinyl sulfathiazole can be evaluated as a local bacteriostatic agent and as an adjuvant in colon surgery, this drug has ordinarily been administered alone. Obviously, it may be advantageous to saturate the general body tissues with another sulfonamide which is readily absorbed from the intestine and so fortify the local action of succinyl sulfathiazole as well as give added protection to surrounding tissues post-operatively. This plan has been followed in a few instances.

Quantitative bacteriologic studies have been confined to the coliform organisms, because (1) *B coli* are constant inhabitants of the gastro-intestinal tract, (2) the coliform bacteria are moderately resistant to the action of the drug, and (3) the cultural characteristics of these organisms permit their quantitative estimation in the complex bacterial mixtures encountered in feces. The profound physical changes occurring in the stools following drug therapy indicate that the bacterial flora is greatly altered. *B proteus*, *alpha Streptococcus fecalis*, and the *Salmonella* group of organisms are not affected. *B aerobacter aerogenes*, while affected, is more resistant than *B coli*. The

Shiga, Flexner and Sonne strains of the dysentery bacilli are highly susceptible to the action of the drug, as indicated by the results of treatment of some 20 cases of bacillary dysentery. All severe cases of the disease have been cured following four days of treatment. The administration of succinyl sulfathiazole to patients with typhoid fever did not seem to alter the clinical course of the specific disease. The distention was, however, relieved, and the usual bowel care and enemata were not required. One patient had perforations of the lower ileum. At operation, three perforations were closed, and cultures made of the contaminating intraperitoneal material failed to grow *B coli*, whereas the typhoid bacillus was grown in pure culture in desoxycholate medium.

DR E P LEHMAN (Charlottesville, Va.) Through the courtesy of Doctor Firor, and the manufacturers, we have had this substance available for a few weeks, and have used it in a small group of patients with and without large bowel lesions. We have made a considerable number of observations on each patient. I would simply like to confirm the statements Doctor Firor has made. There was a very prompt and sometimes a complete drop in the count of coliform organisms in the stool. Also, the absorption, as judged by the urinary output, is relatively low, about 1 or 2 per cent of the amount ingested. The third thing we noted was that the blood levels have not been as high as Doctor Firor reported. With the small group of patients we have had, we have nothing to say about succinyl sulfathiazole as a clinical adjunct, but we are encouraged.

DR L WALLACE FRANK (Louisville, Ky.) I am not going to make any attempt to discuss this paper, but would like to ask a question. I understood Doctor Firor to say that in cases of constipation, and especially in cases of obstructive lesions, the drug cannot, and does not, come in contact with the bowel and hence it is not efficacious. Has the drug been used as an irrigation through a cecostomy wound or through the rectum up to the point of colonic obstruction?

DR WARFIELD M FIROR (Baltimore, Md, closing) Doctor Frank's question I can answer in the affirmative. Any way you can get the drug into the bowel is satisfactory.

I might tell you a story, in conclusion. I received a letter from a former student about a month ago, who is now in another clinic. He said "There is a lot of bad surgery here and I hold you directly responsible. The surgeons feel if they give some sulfaguanidine they can forget all about surgical technic, and they do forget about it, and it is your fault!"

URETERAL TRANSPLANTATION AND CYSTECTOMY[†]

COMPARISON OF RESULTS AFTER EIGHT YEARS

ADDISON G. BRENIZER, M.D.

CHARLOTTE, N. C.

COFFEY,¹ in 1909, before the Southern Surgical Association suggested the submucosal position of the ureter in the bowel to create a valve, in imitation of the course of the common bile duct between the muscular and mucous coats. This suggestion was executed by C. H. Mayo in February, 1912, and immediately began to supplant the former methods and modifications of Maydl, Moynihan, Martin, Stiles and Fowler, who were never able to create a satisfactory type of valve to protect the end of the ureter. Coffey¹ carried out three methods of disposing of the ureteral ends in the submucosal position: (1) The severed ureteral end, one at a time, was immediately transplanted through the mucous membrane into the bowel. (2) Both ureteral ends, armed with catheters, were simultaneously transplanted through the mucosa into the bowel. (3) The ureteral end was tied off, transfixed to the bowel wall, and penetrated by a necrosing suture into the bowel, to later cut through and create a lateral uretero-intestinal anastomosis.

The difficulties encountered by Coffey of passing the necrosing suture into the bowel lumen, a tight or loose suture, the passage of a rigid instrument to the left and past the valves of the human rectum and sigmoid were overcome by Brenizer's² ring and thread in a supple catheter or rectal tube.

This catheter holding the ring and string was passed up the rectum to the site of the necrosing suture, the suture was easily passed into the ring in the rectum, and when the suture was tied down on the ring it held the ureter and mucosae steadily in position. The cutting of the necrosing suture was aided by peristalsis and tugging on the thread and ring.

The first three cases were performed by the transplantation of the ureters, one at a time, by the necrosing suture, and Brenizer's ring and thread method.

The urograms in the last case in this series are pictured soon after transplantation of the ureters and cystectomy and again eight years later. The patient is in good health, has two bowel movements a day, none at night, the abdomen is well supported, but the ureters and pelvis are considerably dilated (Figs. 1 and 2).

Cabot, Walters,⁸ Ladd and Lanman,⁹ and Lower performed an operation similar, but somewhat modified, and, certainly perfected over that of the original Coffey-Mayor procedure. Cabot performed the operation extraperitoneally, while Ladd and Lanman turn the anastomosis behind the peritoneum. Their results offer a formidable argument in favor of their operation. Walters has operated upon 26 cases, with one death, Cabot 20 cases without any mortality, and Ladd and Lanman 32 cases, without a death. Their recent communications with me (September, 1941) show their

[†] Read before the Southern Surgical Association, Pinehurst, N. C., December 9-11, 1941.

remote results, which are remarkably free from urinary infections. However, some of their intravenous pyelograms show a dilatation of one ureter and pelvis or the other. Lanman believes this due to angulation or stricture of the ureter at the site of the anastomosis and says "We feel confident that if the anastomosis is straight and unobstructed, there will be a minimum amount of kidney infection."



FIG 1—Urogram soon after the transplantation of the ureters by the necrosing suture method creating a lateral uretero-intestinal anastomosis.



FIG 2—The lateral anastomosis of the ureter in the bowel has certain disadvantages over the turning of the total caliber of the ureter into the intestine. Obstruction is more apt to occur as evidenced by a dilatation of the ureters and pelvis. Admixture of intestinal contents and urine takes place at the site of the anastomosis and infection is conveyed to the bladder. Finally, the ureteral stumps from the site of the anastomosis to the bladder must be found, tied off and tucked back into the bowel when the cystectomy is performed.

Lanman and Colby¹¹ decry the use of catheters. Priestly formerly transplanted both ureters simultaneously, using short rubber catheters, but tells me now "I did use them for a few years until I felt confident of the technical procedure, but now I am getting along quite satisfactorily without them." Ferguson,³ in his experiments on cats, transplanted a segment of both ureters simultaneously into the rectum and left both ureters connected and running urine to the bladder. Higgins⁴ employed Ferguson's suggestion and Coffey's necrosing stitch, caught through gauze wrapped around a rectal tube. Higgins reported to the writer 52 cases with three deaths and good functional results following his technique. Walters⁸ objected to the necrosing suture, as elaborated by Higgins, saying "In an experimental

study of the so-called aseptic suture necrosis method, Mann and I found that immediate or eventual hydronephrosis occurred so frequently, even though urine appeared in the rectum from the fourth to sixth day in most cases, that I have been fearful to use the method clinically."

The writer could not, so summarily, dismiss the suture necrosis method as did Walters, and employed the simultaneous transplantation of both intact ureters with his ring and thread. There was repeated pyelitis in a colored girl who had undergone a simultaneous transplantation of a segment of both ureters, using the necrosing suture and the Brenizer ring and thread (Ferguson, Higgins, Brenizer). The writer does say, and agrees with Walters and Mann thus far, that operations upon the ureter which do not eventually turn the total caliber of the ureters into the intestine, but depend upon a lateral uretero-intestinal anastomosis, may be followed by partial obstruction at the site of the implant. In addition to this, the flow of urine is not immediately cut off from the bladder and there is an interchange between the lumina of the ureter and intestine, contaminating the urine to the bladder. Also when cystectomy is performed, the ureteral stumps, from the anastomosis to the bladder, must be found and tucked back into the bowel. In spite of these disadvantages, the great majority of these cases, where the necrosing suture was used, have ended well in spite of some dilatation of the ureters and pelvis (Figs 1 and 2, repeated pyelitis in the colored girl).

The fact it was along the route of the necrosing suture that the writer^{5, 6} developed the following method. A segment of both ureters, left connected and running urine to the bladder, was placed in the submucosal position. The ureter was straddled by a hairpin wire, the sharpened ends of which were passed through the intestinal mucosa into a catheter previously inserted into the rectum (Fig 3). And then the muscularis and serosa were closed over the ureter and wire loop. After about eight days, the ureters were cut

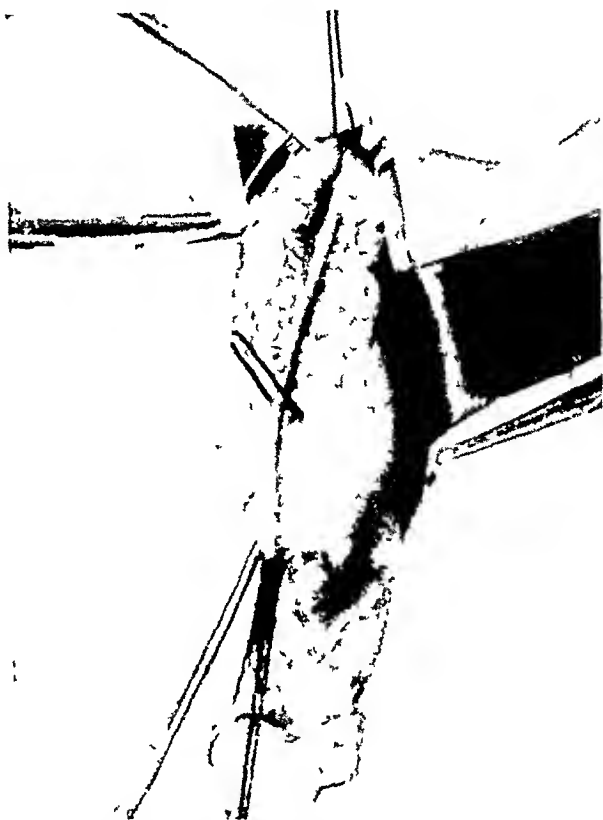


FIG 3—A segment of both ureters is implanted, simultaneously, into the rectum at one abdominal operation. Each ureter is looped over by a long hairpin wire, sharpened on the ends. The ends are made to pierce the mucosa and pass down a catheter, previously inserted into the rectum, until a narrow loop straddling and surrounding the ureter remains. The catheter wire arrangement is left in the rectum for eight days, when the ureter is cut and its total caliber turned into the rectum by the application of an electrocutting current to the wire ends, where they emerge from the catheters at the anus.



Fig. 6—The urogram of the case in Figure 4 shows the ureters and pelvis not more dilated but decidedly improved with time



Fig. 5—Urogram of the case in Figure 4 before operation shows a marked hydronephrosis and hydro-nephrosis

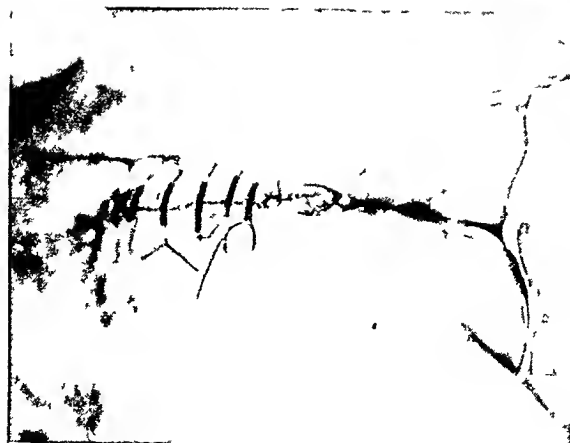


Fig. 4—With both ureteral ends completely turned into the rectum and all urine flow cut off from the bladder, the ureteral stumps to the bladder may be disregarded and the cystectomy made easy. The wide dissection in a sterile field allows a better plastic closure

through and completely turned into the gut by applying an electro-cutting current to the wire ends emerging from the catheter at the anus

An operation similar to the original Coffey-Mayo procedure as performed by Walters, Ladd and Lanman, and Lower, and that by Bienizer,^{5, 6} have two very essential points in common. Both of them, eventually, turn the total caliber of the ureter into the bowel and divert all urine from the bladder



FIG 7—Boy, 17 years, 8 years after transplantation of the ureters and cystectomy for epispadias and incompetent vesical sphincters and repair of the epispadias. At the time of the cystectomy, the seminal vesicles and vasa deferentia were preserved and a rim of bladder was sewn over the prostatic urethra. Due to this vesical pouch, ejaculation and viable spermatazoa have been retained.



FIG 8—The urogram of the ureters and pelvis, 8 years following the operations, shows them to be normal in structure and function. The patient is in good health, has two or three bowel movements a day and he has retained his sexual and procreating functions.

(1) The Bienizer⁶ procedure accomplishes this at one operation. All hemorrhage, edema and lameness of the ureter and bowel which might obstruct, are allowed to subside before the ureter is cut through with an electro-cutting current.

(2) The wound is never exposed to infection by opening the mucosa or piercing it toward the abdomen by a transfixing suture. The ends of the hairpin wire pass from the abdomen through the mucosa into the rectum.

(3) The anastomosis is turned behind the peritoneum. In reality, the incision in the intestine is made to approach and loosely envelop the ureter,

scarcely raised from its bed. The ureter is lifted but not stripped of its blood and nerve supply. With the looser fit of the intestinal mucosa around the ureter, the two structures, by moving up and down or by rotating, can adapt themselves more in line with each other. The stitching of the peritoneal incision to the bowel finally gives it anchorage.

The immediate and ultimate results in the two following cases (Figs 4, 5, 6, 7, and 8), pictured after transplantation of the ureters and cystectomy and then again after eight years, shows them in good health, a couple of bowel movements daily and the intravenous urograms improved, rather than grown worse with time.

At the time the cystectomy was performed on the boy, the vasa deferentia and seminal vesicles were separated from the bladder and a rim of bladder was used to cover the prostate. To the creation of this pouch around the prostate by the writer and the repair of the epispadias, undertaken by Dr R. W. McKay, of Charlotte, is attributed his power of erection, ejaculation and viable spermatozoa. This boy is in excellent health. His urogram is normal after eight years, and he has retained his sexual and procreative functions.

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FINNEY-HOWELL RESEARCH FOUNDATION, INC

At the meeting of the Board of Directors of this Foundation held in February, eight fellowships were awarded for the period of one year. A list of the eight Fellows follows:

- Julius C. Abels, B.S., M.D., to work at Memorial Hospital for the Treatment of Cancer and Allied Diseases, 444 East 68th St., New York City
- Glenn Horner Algire, M.D., to work at the National Cancer Institute, Bethesda, Md.
- Bernard E. Kline, B.S., M.S., to work at McArdle Memorial Laboratory, University of Wisconsin, Madison, Wis.
- Margaret Nast Lewis, A.B., Ph.D., to work at the Crocker Radiation Laboratory, University of California, Berkeley, Calif.
- Alfred Marshak, B.S., Ph.D., to work at Crocker Radiation Laboratory, University of California, Berkeley, Calif.
- Rose I. Shukoff, M.D., to work at the Glasgow Royal Cancer Hospital, Glasgow, Scotland.
- Emilia Vicari, to work at the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine.
- Benjamin Norman Horwitt, B.S., Ph.D., to work at Harvard University, Converse Memorial Laboratory, Cambridge, Mass.

THE TREATMENT OF TRICHOMONAS VAGINALIS VAGINITIS WITH THE LACTOBACILLUS*

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AND
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IT IS with some hesitation that we present another method of treating vaginitis due to trichomonads. Time and further clinical studies have shown, in the case of so many of the methods already advocated, that the claims made for them were unwarranted.

Some one has truly said that a trichomonas infection is an ideal condition to treat in transients. By this it is meant that when an out-of-town patient consults a physician because of an irritating discharge caused by trichomonads he can usually give prompt temporary relief and acquire her gratitude. The trouble is that so often the symptoms return with the next or subsequent menstrual periods.

The return of symptoms with menstruation is due probably to the decreased acidity of the vagina which occurs at this time. In many instances a few trichomonads survive the prescribed treatment and continue to live in the upper vagina, and with the decrease in acidity they increase in number, set up an inflammation, and cause a return of the vaginal discharge.

The importance of these recurring exacerbations of trichomonas vaginalis vaginitis cannot be overemphasized, for in women during menstrual life the trichomonas vaginalis is probably the commonest cause of leukorrhea. There is, in our minds, not the slightest doubt that this statement is true when one is referring to the type of women seen in private practice and, we believe, it is also true for dispensary patients, although gonorrheal endocervicitis in this latter type of patient runs the trichomonas a close second as a cause of leukorrhea. Moreover, the trichomonads must always be thought of and looked for when a woman complains of pruritus and dyspareunia.

Trichomonads cause a vaginitis and little, if any, endocervicitis. The characteristic lesion is most often seen in the upper posterior part of the vagina just behind the cervix. One not infrequently sees in this area minute red spots, giving the upper posterior vaginal wall a strawberry-like appearance.

Some of those who have written about trichomonas infections have stated that the discharge often contains bubbles and is apt to have a slight greenish tint but personally we have seldom observed these peculiarities in the discharge. In our experience there is nothing that is characteristic in the appearance of the discharge. It may be thick or thin, yellow or white. It is, however, apt to cause much more irritation than does the discharge caused by endocervicitis.

* Read before the Southern Surgical Association, Pinehurst, N C, December 9-11, 1941

The trichomonads occasionally invade the urethra, Skene's and Bartholin's glands. Cases of salpingitis, due to the trichomonas vaginalis, have been reported but, although we have seen many hundreds of patients with a leukorrheal discharge due to these organisms, we have never seen a case of salpingitis for which we thought they were responsible.

The trichomonas is a protozoa with actively moving flagella at one extremity and an undulating membrane. The latter cannot always be seen as easily as the flagella. These organisms are larger than an ordinary pus cell and yet smaller than the epithelial cells which line the vagina and which can always be seen in vaginal smears. The trichomonads are very motile. Under the microscope their flagella can be seen moving rapidly. When the protozoa happen to be caught under a mass of epithelial cells they often make the whole clump of cells move.

The diagnosis is made by demonstrating the organisms with the microscope. No special apparatus is needed. All that is required is a little normal salt solution and an ordinary microscopic slide. In some articles you will read that hollow ground slides should be used in studying the trichomonas but they are not necessary. The technic for demonstrating these organisms is as follows. The gloved finger is inserted high in the vagina behind the cervix and a drop of the secretion taken on the gloved finger. This is mixed with a little normal salt solution and the preparation examined at once. The organisms can be seen under low or high grade power. It is not necessary to stain them.

In some women, smears examined in the intermenstrual period may fail to show the organisms, while those taken immediately before or after a period will reveal them. In fact, in some instances the organisms can more easily be demonstrated if the patient is examined when she is actually menstruating.

The diagnosis is often missed for two reasons. The first is the same reason that explains why so many conditions remain undiagnosed. It is that they are not thought of. The second reason that explains why physicians sometimes fail to make the diagnosis is that while they think of trichomonas vaginalis as a possible cause of leukorrhea they think of it two minutes too late. That is what often happens. A woman comes to a doctor complaining of a leukorrheal discharge. He thinks of endocervicitis, polyps, carcinoma and many other gynecologic conditions as being the possible cause of the discharge. He at once puts green-soap or some other lubricant on his fingers and makes a pelvic examination. After his examination has failed to demonstrate any of the conditions mentioned above he then thinks of the possibility of a vaginitis due to the trichomonas vaginalis, takes smears, looks at the material under the microscope and fails to see the organisms. This may be due to the fact that the green-soap on his fingers killed the trichomonas which were in the superficial tissues and by which the diagnosis could have been made. We feel that it is advisable to take smears for trichomonas vaginalis as the first step in the study of all patients complaining of leukorrhea, pruritus, and dyspareunia.

Another factor that sometimes interferes with the diagnosis of trichomonas

infections and also of gonorrhea is that many women through a natural sense of cleanliness will take a douche immediately before coming to a doctor's office and thus prevent the physician from making the diagnosis. It is well to ask every woman who comes to you complaining of leukorrhea when she took her last douche.

Until we began working on the method of treatment which we are now presenting, we had, as most of us have, tried one after another of the usual procedures recommended for trichomonas vaginalis vaginitis. All of them were helpful in some cases. However, as has been the experience of so many gynecologists there were numerous cases in which a recurrence of symptoms occurred following the menstrual periods with a reappearance of the protozoa. Moreover, there were a few patients to whom the treatments did not give even temporary relief.

Although there have been many treatments recommended for trichomonas vaginalis vaginitis, they may be divided into two groups based on what it is hoped the treatment will accomplish. In the first, an effort is made to destroy all the protozoa by the use of antiseptics. Silver picrate, aldisone and carbarsone are among those that have been recommended. Sometimes mechanical cleansing with green-soap or other solutions is added to the use of antiseptics.

In the second group of treatments less attention is paid to antiseptics than to measures which it is hoped will restore the normal defenses of the vagina. They are based on the general idea that it is possible for the protozoa to exist only when the normal mechanism which protects the vagina against infection has been disturbed.

In general, this defense mechanism of the vagina is believed to depend primarily on three conditions. First, that the vaginal secretion remains at its normal low pH , second, that the Doderlein or vaginal Lactobacilli are present in sufficient numbers to form lactic acid and finally that there is sufficient carbohydrate, perhaps in the form of glycogen, in the vaginal epithelial cells or spaces between the cells to afford adequate nourishment for the continued growth and activity of the Doderlein bacilli.

With the idea that in vaginitis acid douches might restore the bactericidal power of the vagina, lactic acid and vinegar douches have been prescribed in trichomonas vaginalis. They do give the patient considerable relief but apparently are not sufficient, in themselves, to completely correct the condition. Few if any cures have been brought about by simply using acid douches.

Adair and Hesseltine believe that, in the treatment of trichomonas vaginalis vaginitis, the most important therapeutic measure is to furnish sufficient nourishment to maintain a normal bacterial flora and, hence, they recommended, in 1936, that vaginal tablets containing 95 per cent lactose and 5 per cent citric acid be used. Karnaky with the same idea became enthusiastic over the use of vaginal suppositories, containing lactose and dextrose. The preparation which Karnaky recommended, and which was placed on the market under the trade name of floraquin, does also contain an antiseptic.

known as diodoquin but the antiseptic is thought to have less therapeutic value than the sugars

We have used floiaquin in a large number of cases, with some satisfactory results. However, there were in the series of patients quite a few who continued to harbor the parasites in the vagina and to have recurrences of leukorrhea and pruritus with the menstrual periods. Being rather discouraged by the results obtained from the numerous preparations that had been recommended for the treatment of vaginitis due to the trichomonas vaginalis we decided to attempt to build up the vaginal defense by simultaneously carrying out several measures. Not only was nourishment suitable for the growth of Doderlein's bacillus to be introduced into the vagina but also viable Lactobacilli.

Such a procedure if feasible seemed worth trying. To quote from Hessel-tine on an article dealing with trichomonas infestations: "One thing is well established and that is with the restoration of the vagina to a normal cellular and bacteriologic flora the disease entity vanishes."

Since the time when Metchnikoff proposed the ingestion of *Lactobacillus bulgaricus* as an "elixir of life" to the more recent work of Rettger and many others, aciduric bacteria have enjoyed periodic popularity as agents for the relief of certain human ailments. Within the last two decades, "acidophilus therapy" has soared and fallen. It was used principally for the relief of gastrointestinal symptoms and depended upon implantation of the organisms in the intestinal tract with subsequent elimination of other, less desirable, types of bacteria. The literature from 1910 to 1930 contained a great deal of evidence that such therapy was justified. On the other hand, its popularity as a panacea has been rightfully questioned. When indicated, massive doses have doubtless given desirable results. It is not our purpose to take issue with either view in the discussion which arose in this respect. There can be no doubt that many commercial preparations during the heyday of acidophilus therapy were of little or of no value due to the lack of viable Lactobacilli.

Perhaps, however, some of the unfavorable reports, such as those by Bass and James, on *Lactobacillus* preparations were in part due to media difficulties for, as will be brought out shortly, we had in the beginning of this work considerable trouble in growing Lactobacilli on the usual solid medias. Moreover, James, in a recent personal communication, has expressed the opinion that conditions in the intestinal tract and in the vagina are so different it is not surprising that we have been successful in implanting Lactobacilli in the vagina.

Our first attempts to treat trichomonas vaginalis vaginitis with lactic acid-forming bacilli plus sufficient carbohydrate for the nourishment of the bacilli were rather crude. The junior author, who at the time this work was started, was the Bacteriologist to the Gynecological Department of the Johns Hopkins Hospital, had a culture of *Lactobacillus* which had been obtained from the United States Department of Agriculture. The culture secured from Washington is known as Hansen's strain, and has been used throughout this investi-

gation Two lumps of ordinary sugar were coated with this culture and placed in the vagina Quite naturally the heat of the tissues soon melted the sugar, converting it into syrup which ran out of the vagina Tampons made of ordinary cotton were of no help as they quickly absorbed the syrup and prevented its coming in contact with the vaginal epithelium Tampons made of nonabsorbent cotton were then used, with more success In fact, many women obtained prompt relief by this crude treatment

Encouraged by these results we then endeavored to work out a simpler method of carrying out this treatment Tablets were then prepared for us under the careful supervision of Dr John Brewer, Bacteriologist for Hynson, Westcott and Dunning The tablets are prepared in the following manner

Sterile skim milk is inoculated with a culture of *Lactobacillus bulgaricus*, U S D A Hansen's strain After 48 hours' incubation, 1,000 cc of this culture is mixed with 325 grams each of XXXX sugar and milk sugar This is thoroughly dissolved in the milk and the mixture is spread in thin layers on enamel pans and dried in a vacuum oven at 37° C

The mixture is scraped from the pans, broken into bits, and replaced in a drier to complete desiccation When completely dried six cubic centimeters of white mineral oil and 38 Gm of starch are added The mixture is then pressed into tablets The finished tablets weigh 1.3 Gm, and represent 1.25 cc of original culture

We were, of course, interested in determining the number of live *Lactobacilli* to the tablet Tomato juice agar, using the formula of Valley and Heiter, and also dehydrated tomato juice agar (Difco) was not found to be satisfactory for this purpose On the other hand, it was possible to prove the presence of viable organisms in milk and tablets when dilutions were made in tubes of litmus-milk and later in thioglycolate medium By this method we were able to determine the number of living organisms in a tablet or in one cubic centimeter of the milk culture Dilutions were made by placing one tablet into 10 cc sterile water One cubic centimeter of this, when dissolved, was transferred to a tube containing nine cubic centimeters of sterile water, one cubic centimeter of this dilution transferred to a second tube containing nine cubic centimeters, and so on One cubic centimeter of each dilution was transferred to 10 cc of thioglycolate medium or litmus-milk, making the final dilution from the first tube, one tablet per 100, second tube, one tablet per 1,000, etc Growth of the *Lactobacilli* was determined by coagulation of the milk or clouding of the thioglycolate medium, and Gram's stain of these media after 24 hours' incubation showing presence of typical gram-positive bacilli

By this procedure we have determined the approximate number of viable *Lactobacilli* in tablets kept for as long as 12 months Numerous samples taken from different lots of tablets all showed between 10,000 and 100,000 viable *Lactobacilli* in each tablet after they had been stored in a refrigerator for 12 months

It is of interest, and possibly important, to note that in no case were contaminating organisms found in or on any tablets tested, in spite of the fact

that no precautions were taken, during storage, to maintain sterility. This, of course, may be explained on the basis of the acidity of the original milk cultures used in making the tablets.

These tablets have been used in several different ways, and it may be that the best way has not yet been worked out. However, the method which we are employing at present is the following. As soon as the diagnosis is made a bivalve speculum is introduced into the vagina, the cervix inspected for complicating endocervicitis and Skene's and Bartholin's glands inspected for possible involvement. The vagina is then dried with cotton and two *Lactobacillus* tablets inserted high in the vagina in the posterior fornix behind the cervix. The vaginal orifice is then plugged with a tampon of nonabsorbent cotton. When the patient returns on the next day the tampon is removed, material taken from the vagina for microscopic study and the treatment carried out on the preceding day repeated. On this second visit practically every patient will report that the itching has been much less, and it is very unusual to be able to demonstrate organisms at this time.

Such office treatments are repeated daily for from four to six days. The patient is then told to insert one *Lactobacillus* tablet high in the vagina each night. She is told to take douches only if she becomes uncomfortable from unabsorbed particles of the tablets coming out of the vagina and causing irritation. A white vinegar douche (5 per cent acetic acid) is recommended in a strength of from two to four tablespoonfuls to two quarts of water. Two douches a week are usually sufficient.

This home treatment is continued from three to six weeks and longer if necessary. However, if the organisms promptly disappear and show no immediate tendency to recur, the tablets need be used only every other night. It is especially important that they be used while the patient is menstruating, as that is, of course, the time when the vaginal defenses against the trichomonads are weakest.

If there is an endocervicitis which in itself is producing some of the leukorrhea it is treated by a cauterization. All patients are given the usual instructions regarding toilet technic, just as should be given no matter what method of treatment is being carried out. This consists of instructing the patient to clean herself, after defecation, from in front backwards, that is from the vagina towards the rectum, rather than in the reverse manner as is usual in most women. This lessens the likelihood of the condition being kept up by constant reinfection from the anus. When it is possible to clear up the infection quickly it is better to advise against sexual relations. When the treatment must be continued for a longer period of time the patient is instructed to take a plain water douche before coitus.

Unfortunately, some dispensary patients cannot come for daily office treatments during the first week after the diagnosis has been made, and in these cases we have to rely largely on the home treatments carried out by the patients themselves. We have not given patients tampons of nonabsorbent

cotton with which they themselves might plug the vaginal orifice, although this might be advisable

These tablets have now been used on 50 consecutive, unselected cases. Thirty-one were white women, 19 colored. There were two children in the series, age six and seven, respectively, and two women beyond the menopause. The remaining 46 were in the reproductive age.

Just a few days ago a five-weeks-old child was brought into the dispensary with a profuse leukorrheal discharge which was thought to be gonorrheal in origin. However, smears for gonococci were negative while examinations for trichomonads showed a large number of the protozoa. Because the vagina was so small we have had difficulty in getting the Lactobacilli into it. However, we have been fairly successful with some long, very narrow tablets. Perhaps suppositories would be more effective, but their preparation has not yet been completed. After two treatments the discharge almost entirely disappeared, although there are a few organisms still present. This is, I believe, one of the youngest cases of vaginitis due to the trichomonas vaginalis which has been recorded. It is of interest that the mother also has a vaginitis due to the trichomonas vaginalis, indicating that the child probably acquired the disease from the mother.

All 50 of the women in our series complained of a vaginal discharge, 40 of pruritus vulvae and ten of dyspareunia. Fifteen had received treatment for the trichomonas infestation before coming under our care. Thirty-seven had had symptoms for over six months before we saw them, and 25 for a year or more. In our series there were only four patients whose symptoms were only a few weeks' duration.

This paper is essentially a report of the results obtained by the use of tablets containing Lactobacilli and not a detailed clinical study of vaginitis due to the trichomonas vaginalis. However, we wish to state that on the basis of our observations we are in complete accord with those investigators who in the past few years have brought out the fact that trichomonads not infrequently cause an inflammation of the Bartholin glands. This is a point of sufficient importance to deserve being stressed. Until a few years ago many gynecologists taught that when an examination showed bilateral thickening of the Bartholin glands one could be almost certain that at some time the woman had had gonorrhea. This is incorrect. Shelanski and Savitz, in 1939, reported that they had demonstrated trichomonads in Bartholin's and Skene's glands, and proved conclusively that an inflammation of these glands may be due to trichomonads. In our series there were several cases of Bartholinitis, in all probability due to the trichomonas vaginalis. In one patient, an unmarried woman with a hymen which would not admit the tip of the finger, the glands reached the size of olives. One case in our series interested us especially. Trichomonads were persistently present in the voided specimen of urine, while smears taken from the walls of the vagina showed no protozoa. After several examinations the trichomonads were found to be coming from an infected Skene's duct.

We realize that a series of 50 cases is not large enough to draw any very definite conclusions from regarding the efficacy of a method of treatment. Nevertheless, we do feel that our results warrant this preliminary report of the work we are doing.

Every patient treated with the *Lactobacillus* tablets showed immediate improvement and in many instances the organisms disappeared at once. Nevertheless treatment was continued from three to six weeks and when necessary longer. There have been recurrences in six patients whom we had thought were cured, perhaps in some instances these were reinfestations. Usually the supposed recurrence cleared up more rapidly than did the first infestation.

Forty-eight out of the series now have negative smears, and are asymptomatic. Both of the patients with positive smears are women in whom recurrences or reinfestations recently developed. They are now being treated.

All the patients whom we have considered cured have been instructed to report for examination immediately at the termination of each menstrual period, and without taking a douche before coming for examination. Thirty-five patients have remained symptom-free and have shown persistently negative smears for three months. We have 20 patients who are apparently well after six months.

We are enthusiastic about the prompt results which we have obtained with the *Lactobacillus* tablets, and we have had numerous patients go without treatment for from three to six months in order to prove that they have really been cured of the infestation. Nevertheless, we feel that every woman who has had a trichomonas infection should continue for considerable time to take either acetic acid douches or to use the *Lactobacillus* tablets for a few days each month around the time of the menstrual period. In fact, no matter what treatment is carried out for vaginitis due to the trichomonas vaginalis it should, in our opinion, be repeated at each menstrual period for from six months to a year.

There is still a great deal to learn about the trichomonads. Perhaps what we need is not a more effective way of treating this condition but to learn the necessity of treating it for a longer period of time than we have in the past. It is possible that the organisms, when attacked by various antiseptics, develop a few very resistant forms with the power to live much longer than the ordinary trichomonads.

There are of course certain questions that at once present themselves when one considers the advisability of using lactic acid-forming bacilli in vaginitis and some of these we hope to answer in the near future. For instance while we have clinical results to report which indicate the effectiveness of the method which we have used, and are also able to prove that the tablets themselves contained great numbers of viable lactic acid-forming bacilli, even when refrigerated 12 months, we have not shown just how rapidly these tablets restore the vaginal flora to its normal state.

We have analyzed the bacteriologic flora of a series of women, and

selected six from whose vagina it was impossible to grow any Lactobacilli. These six were instructed to insert one Lactobacillus tablet in the vagina every night for six nights and then to report for examination 48 hours later. Five of these six were then shown by culture to have large numbers of viable Lactobacilli in the vagina.

SUMMARY

A method of treating vaginitis due to the trichomonas vaginalis is presented. It differs from other methods in that viable lactic acid-forming bacilli are introduced into the vagina. There have been a few recurrences or reinfections, but in all cases the method has yielded almost immediate relief of symptoms and in the great majority of instances the vaginas have remained free of trichomonads. Many of these patients have now been followed for six months.

We realize that much additional clinical and laboratory work must be carried out to establish, definitely, the value of Lactobacillus therapy in the treatment of vaginitis due to the trichomonas vaginalis. In spite of the relatively good results which we have obtained we do not claim that this method of treatment will completely eliminate recurrences in all patients. However, we feel our results justify this preliminary report.

The authors wish to express their appreciation to the Hynson, Westcott and Dunning Co. for their cooperation in this work.

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ACOUSTIC TUMORS

WITH SPECIAL REFERENCE TO END-RESULTS AND
SPARING OF THE FACIAL NERVE

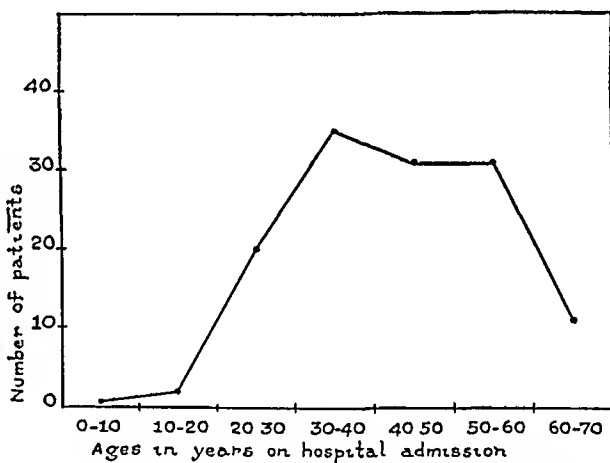
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IN A RECENT PRELIMINARY REPORT on acoustic tumors, Olivecrona¹ stated "The problems have shifted insofar as we are now not so much concerned with the immediate mortality, which has been reduced to reasonable proportions, but with the late results" With this in mind, the purpose of the present study is to give the late results in Olivecrona's entire series of acoustic tumors from 1930 to 1939 In addition, a detailed description of the operative technic of saving the facial nerve during radical removal of these tumors is presented, together with certain further points of diagnostic and clinical interest

The material consists of 130 cases of verified acoustic tumors, operated upon between June, 1930 and June, 1939 In every instance microscopic examination of the growth proved it to be a neuroma An additional number of 34 cases of acoustic tumor, previously verified by operation, and reported by Olivecrona in 1934,² will not be considered in the present study except in the discussion of mortality statistics where the material then published is carried up to date Finally, it may be mentioned that three cases of bilateral acoustic tumor, also not here included, were previously verified by operation, and two of these were reported by Olivecrona in 1928³



Graph 1—Representing the ages on admission, plotted by decades

Age—Graph 1 represents the ages on admission, plotted by decades It may be seen that the greatest number of patients came under observation during the age-period of 30 to 40 years The youngest patient was 18 years of age, and the oldest 68 The average age of the 130 patients is 42.3 years It is interesting to note that in Doctor Cushing's series of 190 neuromata the average age is approximately the same, that is, 40 years *

Sex—There were 79 females (60.8 per cent) and 51 males (39.2 per cent) This incidence of approximately 60:40 among the sexes in Doctor Olivecrona's series is also close to that in Doctor Cushing's series of 190 neuromata, in which the corresponding figures are 122 females (64.2 per

¹ Personal communication from Dr Louise Eisenhardt, Brain Tumor Registry, Yale University School of Medicine, New Haven, Conn

cent) and 68 males (35.8 per cent).⁴ Another interesting point, to which attention has already been called, is the possible significance of the fact that there is the same definite predominance in the incidence of meningioma in females over males, the proportion being 60:40 in a series of 313 cases.⁴

Symptoms and Signs—The chronology of symptoms and signs in cases of acoustic neuroma, as established by Cushing,⁵ is as follows:

- (1) Auditory and vestibular disturbances
- (2) Occipitofrontal headache with suboccipital discomfort
- (3) Incoordination and instability
- (4) Evidence of involvement of adjacent cranial nerves
- (5) Signs of increased intracranial pressure with choked disks
- (6) Dysarthria and dysphagia
- (7) Cerebellar crises and respiratory difficulties



FIG. 1.—Case 737 Showing patient two years and five months after complete extirpation of neurinoma with preservation of the facial nerve.

To-day, these progressive, characteristic symptoms and signs are so well recognized in the average case of acoustic neurinoma that they need not be considered in further detail here.

Occasionally, however, in a somewhat atypical case, the diagnosis may be obscure, and ventriculography becomes necessary. This occurred in four instances in the present series, one of which may be briefly described as follows:

Case No. 24037—Admission of female, age 29, complaining of moderate headache of five years' duration. For four years there had been diminished hearing, bilaterally, with tinnitus in the right ear. For two years vision had been failing, advancing to blindness on the left. For two weeks there had been slight clumsiness of left hand.

Examination showed bilateral choked disks, with blindness on left and markedly lowered vision on right. There was no nystagmus. Hearing was markedly diminished, bilaterally, and there was slightly diminished caloric reaction on the right. No definite cerebellar disturbances were present. Roentgenologic examinations of the internal acoustic poruses were negative.

The preoperative diagnosis was uncertain, partly because the deafness was bilateral and the adjacent cranial nerves were uninvolved, and partly because of a poor history due to language difficulties. *Tentative Diagnosis*: Pinealoma or intraventricular meningioma.

Only by ventriculographic study was the lesion disclosed. Dr. E. Lysholm's report is as follows: "There is evidence of a high degree of pressure, with symmetrically internal hydrocephalus including the third ventricle. The fourth ventricle is slightly dislocated dorsally and somewhat to the left. There is a filling defect on the right side of the fourth ventricle. Roentgenologic examination shows the picture usually seen in cerebellopontine angle tumor."

At operation both cerebellopontine angles were investigated, but tumor was found to be present on the right side only.



FIG. 2—Case 240-37. Photographs taken 18 months after complete extirpation of tumor with preservation of the facial nerve.

FIG. 3—Case 240-38. Patient 14 months after complete removal of neurinoma, with preservation of the facial nerve.

Another deviation from the usual chronologic, progressive syndrome of acoustic neuroma is represented by those cases in which normal or nearly normal hearing and normal caloric responses are present. There are several such examples in the present series. In these cases one of the divisions of the eighth nerve (vestibular) is usually uninvolved and occasionally even both divisions are found to be intact. Thus in Case No. 478-37 it is specifically mentioned in the clinical record that vestibular function was intact and hearing normal, bilaterally, although at times the patient had experienced noises in one ear. Unfortunately the weight of this tumor was not recorded, but the fact that bilateral choked disks were present indicates that the growth was large enough to cause obstruction to the flow of cerebrospinal fluid.

Smaller asymptomatic acoustic neuromata have been reported in the literature. In an examination of serial sections of the temporal bone in 250 unselected cases, Hardy and Crowe⁶ found, in five instances, a typical acoustic neuroma deep in the internal auditory canal. These tumors were too small to cause clinical symptoms.

It may be of interest at this point to note which cranial nerves were found to be involved by the neurinomata in this series. They are listed in order of frequency of involvement as follows:

ORDER OF FREQUENCY OF CRANIAL NERVES INVOLVED		
Nerves Involved	No. of Cases	Per Cent
1. Acoustic (cochlear division)	129	99.2
2. Acoustic (vestibular division)	118	90.8
3. Trigeminal	92	70.8
4. Optic (diminished vision)	72	55.4
5. Facial	71	54.6
6. Abducens	16	12.3
7. Glossopharyngeal and vagus	7	5.4

The rarity of glossopharyngeal involvement is remarkable considering the intimate relation of acoustic tumors to this nerve. However, it may be pointed out that patients are not aware of loss of function of the ninth nerve, a fact we often have had opportunity to verify in cases in which this nerve had been severed for relief of glossopharyngeal neuralgia.

Although, subjectively, the patients themselves are unaware of any loss of function following section of the glossopharyngeal nerve, objectively, anesthetic areas are to be found homolaterally in the tonsillar fossa, pillars and uvula. That clinical records often fail to mention any sensory loss in cases in which the ninth nerve has been severed may be due to the difficulties in detecting such loss. Most authors agree that sensory changes occur and that motor function remains unaltered.

Another important point is the presence or absence of nystagmus. In this series of 130 cases nystagmus was present in 125 cases, or 96.2 per cent. It is generally agreed that nystagmus may result from a lesion involving the cortico-cerebellar pathways. Since the corticocerebellar fibers pass from the cortex to the cerebellum by way of the middle cerebellar peduncle, it seems reasonable to assume that absence of nystagmus is a favorable sign, indicating that there is little, if any, compression of the brain stem. Other fibers in the brain stem which give rise, if injured, to nystagmus are the cortico-oculomotor fibers after leaving the Deiters' nucleus as well as the ascending fibers of the posterior longitudinal bundle.⁷ Here again, absence of nystagmus may mean that these fibers have been spared and, consequently, a tumor causing no nystagmus may be considered to be a more favorable one.

In the present series brain stem compression as evidenced by choked disks was present in 90.8 per cent and, as mentioned above, nystagmus was present in 96.2 per cent. A few cases showed neither nystagmus nor choked disks. This further strengthens the probability that nystagmus and brain stem compression may be related phenomena—the latter responsible for the former. However, an occasional case will show no nystagmus in the presence of frank choking of disks, indicating that other factors than brain stem compression probably play a rôle in the production of the type of nystagmus observed in cases of acoustic neurinoma.

Roentgenologic Diagnosis—An examination of the pons acusticus internus to detect possible enlargement from pressure atrophy was made in all of the 130 cases. It was found that some degree of enlargement together with a rather typical funnel-shaped appearance, with or without destruction of the pyramid, was present in 106 cases, or 81.5 per cent. In four cases, one of which has been briefly described above, ventriculographic studies were made because the history and the neurologic findings were atypical. In each of these four cases the diagnosis of a cerebellopontine angle tumor was made chiefly on the basis of the roentgenologic findings.

Operative Technique—With only three or four exceptions all of the operations in this series of 130 cases were performed by Doctor Olivecrona. In 75 cases there was complete extirpation of the tumor with its capsule. In 27

cases the extirpation was subtotal. In 28 cases an intracapsular enucleation of the tumor mass was done. The definition of these different types of operations for acoustic neuromata, as carried out by Olivecrona, may be stated as follows:

(1) *Complete Extirpation*—An operation with total removal of all macroscopically visible tumor.

(2) *Subtotal Extirpation*—An operation in which radical removal had been attempted but found impossible to carry out, usually because of technical difficulties due to a very friable capsule and comparatively firm adhesions to the pons.

(3) *Intracapsular Enucleation*—An operation which is deliberately incomplete.

As seen above, by far the greatest number of cases have been treated by *complete removal* of the tumor, with its capsule, the operative technic of which is as follows:

Operative Technic—The patient is placed horizontally, with the face down, on the operating table, to which are attached special shoulder- and head-rests.

Local anesthesia, preceded by luminal and morphine in small amounts, is the method of choice. This is particularly to be desired because the operator then can follow the fate of the facial nerve during the entire operative procedure, a matter of great importance, as will be discussed later. The pain elicited from the cranial nerves to which a tumor may be attached may be abated or entirely avoided by placing pledgets of cotton moistened with 2 per cent procaine solution on the respective nerves, especially the trigemini.

Unilateral exposure of the cerebellar hemisphere, as advocated by Dandy⁸ in 1934, retaining a narrow bony rim at the foramen magnum, suffices. A resection of the lateral third of the cerebellar hemisphere has been found unnecessary, good exposure usually being obtained by means of de Martel's self-retaining retractor combined with rotation of the operating table about an horizontal axis in the proper direction. As a rule, the ventricular pressure is diminished by puncture of a posterior horn of the lateral ventricle, the needle being left in place during the entire operation. The dura is then opened, the posterior or medullocerebellar cistern, if present, is emptied, and following the opening of the lateral pontine cistern, the tumor is exposed. A small area of the exposed surface of the tumor is coagulated, and the mass of tumor within its capsule removed with spoon and suction, as in the usual intracapsular enucleation.

In Olivecrona's own words the complete extirpation is now carried out as follows:

"It is essential to push the process of intracapsular enucleation as far as possible in order to obtain ample room for the maneuvers that follow. To safeguard against perforation of the capsule on the ventral side and possible injury to the facial nerve, it is customary to have a nurse observe the face of the patient at frequent intervals. If the operator gets too near the nerve, twitching of the face occurs and further removal of tumor in this particular region should then be abandoned.

"The first step in the removal of the capsule is the mobilization of its lower pole. The glossopharyngeal, vagus and accessory nerves are gently stripped from the lower pole, to which they are sometimes slightly adherent. The nerves are always elongated and dislocated by the tumor, and it is a matter of surprise that functional loss in the region of these nerves is rarely observed.

"An important blood vessel running to the tumor is often seen between or ventral to the above-mentioned nerves. This little artery is a branch of the vertebral and should be doubly clipped and cut.

"While the cerebellum is being held aside by de Martel's automatic spatula, the operator now pushes the lower pole upwards by means of a narrow brain spatula, and a search for the facial nerve is begun. The nerve is most easily found near its emergence from the brain stem, and it is usually possible to recognize it as a flattened band of nerve tissue running alongside the brain stem for a few millimeters before it disappears below the ventral surface of the tumor. When the nerve is seen, its identity is confirmed by faradic stimulation. While the patient's face is under constant observation the nerve is gently mobilized from the ventral surface of the tumor. This is easily done until one reaches a point about half way between the brain stem and the porus, where rather firm adhesions between the facial nerve and tumor capsule are often encountered. It may also be difficult to keep the nerve in full view at this point, and it may be necessary to reduce the bulk of the tumor by further intracapsular manipulations. The course of the facial nerve is rather variable. In most cases it runs fairly straight on the ventral surface of the tumor between the emergence from the brain stem and the porus, in other cases it may be pushed so far in an anterior direction as to be more on the anterior than on the ventral surface of the tumor. In such instances it enters the porus at the anterior margin instead of the usual point of entrance at the posterior, inferior margin. If the facial nerve disappears from view it is usually advisable to mobilize the tumor from the porus so that the nerve may be identified at its point of entrance into the porus.

"The neoplastic tissue present in the porus can usually, after firm adhesions present alongside the superior margin of the porus have been separated by sharp dissection, be cleanly enucleated from the porus by a blunt instrument, such as a dissector. On the ventral side the facial nerve is separated from the capsule of the tumor by a thin sheath of arachnoid, the presence of which makes it possible to mobilize the lateral stalk of the tumor from the porus without injury to the facial nerve. If the nerve is not seen at its point of entrance into the porus it can easily be localized by means of faradic stimulation. The nerve is then dissected free from the capsule from outwards inwards until the nerve is completely free from the capsule in its entire course. The removal of the capsule should not be attempted until the dissection of the facial nerve is complete, otherwise the nerve is usually torn at some point where it is adherent to the capsule.

"The last adhesions between the tumor and the porus are now separated. The petrous vein, which is always encountered along the superior, anterior margin of the porus, is clipped or coagulated and divided. The trigeminal nerve is separated from the tumor by the same layer of arachnoid that separates the capsule of the tumor from the facial nerve. Adhesions between the capsule and the trigeminal nerve are rarely encountered and usually the nerve can be stripped from the capsule without difficulty.

"All important nerves now being out of the way, the capsule may be removed. This should, whenever possible, be undertaken from outside inwards, i.e., the lateral stalk of the tumor is grasped with a broad-bladed forceps and gently pulled in dorsal and medial directions. Between the emergence of the fifth and the eighth nerves from the brain stem the tumor is usually more or less embedded in the pons. While pulling at the tumor the pons is gently stripped from the surface of the tumor, and the vessels coming from the basilar artery are clipped and divided as they are encountered. If the capsule is reasonably tough this procedure is usually carried out with ease and without injury to the brain stem, and the whole of the capsule comes away in one piece. Sometimes, however, the capsule is very friable and breaks when the operator tries to pull on it. In such cases it is usually necessary to remove the capsule in numerous small fragments. Even this may be impossible on account of firm adhesions between the brain stem and the tumor. As a last resort a broad brain spatula is inserted between the tumor and the cerebellum and an attempt made to dislocate the tumor from within outwards. This must be done with the greatest care in order not to damage the brain stem, and the attempt should be abandoned if too firm adhesions are encountered. However, with increasing experience it has been found possible to remove the tumor in practically every instance where a radical operation was indicated.

"Following removal of the tumor there is surprisingly little bleeding in the cavity, and what hemorrhage there is usually comes from veins on the lateral surface of the pons. Occasionally one or two bleeding points must be sealed with the cautery, but as a rule a few minutes' packing with pledgets wet in hydrogen peroxide is all that is necessary to insure complete hemostasis. The dura is then carefully closed and the wound sewed up in layers in the usual manner.

"The same technic, as just described, was employed in the cases of subtotal removal, with the exception that fragments of the tumor were left behind attached to the pons.

"The technic of intracapsular enucleation is carried out as described above up to the point where the tumor is exposed, then the capsule must be mobilized from the cerebellum as far as possible. It can be pulled out from its bed in the cerebellum a good deal, after gradual removal of its contents by suction curettage. In this way the upper pole is gradually dislodged sufficiently out of the incisura tentorii to reestablish the fluid pathways, which is very important. The curetting can also be done much more completely because of better visibility. In the olden days the tumor was left entirely in place and a very large part usually remained alongside the pons and most of the upper pole."

COMMENT—In almost all cases of acoustic neuroma one or the other of the three types of operation described above is carried out. However, occasionally a cystic neuroma is encountered and here a radical procedure becomes unnecessary, for it suffices to empty the cyst, remove tumor fragments which are present in the cyst wall, and cauterize the cavity with Zenker's solution or some other agent. As far as we know, cystic neuromata have no tendency to recur, a fact that has been observed in following up three patients operated upon by this less radical method prior to June, 1930, all still symptom-free in June, 1939.

The choice of operative procedure depends also on a number of other factors, such as age, sex, physical and mental health, and social position of the patient. From a technical standpoint it must be kept in mind that secondary operations are more hazardous than primary ones, since the presence of scar tissue entails greater danger to the pons and, in addition, renders the saving of the facial nerve well-nigh impossible. Consequently, the post-operative course may become more complicated and the morbidity increased. An attempt at radical removal, therefore, should be made in all cases except those in which the tumor is cystic or the patient's life expectancy is short, due to old age, social conditions, hypertension, or other systemic illness. Such an attempt does not mean that the facial nerve is necessarily endangered, because the decision as to whether or not to proceed radically is not made until the lower pole has been mobilized and the stalk divided at the internal acoustic porus, *i e.*, before any harm has been done to the facial nerve. If technical difficulties make it impossible easily to preserve the facial nerve, and its preservation is imperative because of the individual or social aspects of the case, then a bridge of tumor tissue covering the facial nerve from the porus to the pons is left behind, all other visible tumor being removed. This type of incomplete operation was recently carried out in an elderly male with hypertension. Further discussion of the preservation of the facial nerve will follow later.

Table I shows the frequency of the three types of operation in different years expressed in percentages

TABLE I
TYPES OF OPERATIVE PROCEDURES AND THEIR RELATIVE FREQUENCY

Year	No of Cases	Intracapsular Enucleations*	Subtotal Extirpations	Complete Extirpations
1930-1931	10	80 0%	0 0%	20 0%
1932-1933	36	16 7%	16 7%	66 6%
1934-1935	31	6 5%	29 0%	64 5%
1936-1937	28	32 1%	21 4%	46 5%
1938-1939	25	12 0%	24 0%	64 0%

* No intracapsular enucleation was done in 1939

Table I indicates that, except during the first two years, the radical approach with complete extirpation was the favorite one in this clinic

Postoperative Course—The postoperative course of the patients presented no unusual features. It may be mentioned, however, that in one instance (Case 244 38) a postoperative hemorrhage occurred. It so happened that in this particular case the facial nerve, which was severed during the operation, had been sutured. Subsequent reopening, with evacuation of blood clot, resulted in new tearing of the sutured facial nerve and complete facial paralysis ensued. In no other case was the facial nerve sutured in the posterior fossa, and it was unfortunate that the postoperative hemorrhage thus prevented the study of the effectiveness of reunion of the facial nerve. However, it seems reasonable to assume that, barring accidents, such as mentioned above, the suture should have resulted in complete restoration of facial function, particularly when one takes into consideration the recent thorough work of Tarlow,⁹ who states that the transitional glial zone of the seventh nerve extends less than 1 Mm beyond the exit from the pons, or 0.8 Mm, to be exact.

End-Results—The statistical material on end-results is based upon answers to a questionnaire sent to all surviving patients in May, 1939. A prompt reply was received from 82.3 per cent of the patients. In practically all of the remaining cases the records of the end-results were obtained from letters received within the preceding two months or through personal interview. A few patients residing in distant parts were not heard from within this period.

The questionnaire covered essential points relating to cerebellar disturbances, such as difficulty in walking, involvement of the cranial nerves, particularly of the facial, muscular weaknesses, and, above all, the earning capacity of the patient. In 39.2 per cent of the cases the patients cooperated to the extent of sending photographs of themselves to show the present state of facial nerve involvement.

List,¹⁰ in a paper on acoustic tumors, has divided his material into four groups, each group representing a certain developmental stage of the disease. In our series most of the cases happen to fall in the fairly advanced group described by List as Stage III, since the roentgenologic examination showed changes at the internal acoustic porus in 81.5 per cent, and choked disks were

present in 90.8 per cent of the 130 cases. It has seemed more desirable, therefore, in the present study to divide the material into three groups according to the particular operative procedure employed. The end-results in each group will be discussed, with emphasis placed upon the following: (1) Mortality, (2) facial paralysis, and (3) earning capacity.

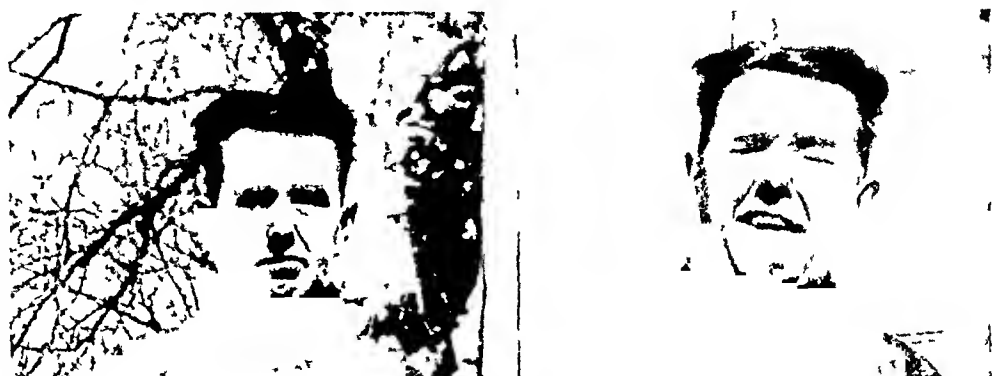


FIG. 4.—Case 48238. Showing patient 10 months after a complete extirpation, with preservation of the facial nerve.

(1) *Mortality*—The total number of operations was 133 in the 130 cases. In Case 29731 an intracapsular enucleation preceded a complete extirpation, and in Case 251835 two subtotal operations had been carried out before the tumor was finally removed radically. The results are shown in Table II.

TABLE II
MORTALITY STATISTICS IN 130 CASES OF ACOUSTIC NEURINOMA

	No of Cases	No of Operations	Operative Mortality	Case Mortality	Late Mortality
Complete extirpation	75	75	(14) 18.7%	(14) 18.7%	(4) 6.6%
Subtotal extirpation	27	29	(6) 20.1%	(6) 22.2%	(1) 4.8%
Intracapsular enucleation	28	29	(8) 27.6%	(8) 28.6%	(4) 20.0%

The higher operative mortality percentage among the intracapsular enucleations may be explained by the fact that this procedure was most often undertaken during the early years of the clinic (*cf.* Table I).

At this point it may be of interest to refer to the mortality statistics of the first 34 cases of intracapsular enucleation, as reported by Olivecrona, at the Third International Neurological Congress, in Copenhagen, in 1939 (Table III). These cases, as has been pointed out, are not included in the present series.

TABLE III
MORTALITY STATISTICS IN 34 CASES OF INTRACAPSULAR ENUCLEATION
OPERATED UPON PRIOR TO 1930

	No of Cases	Operative Mortality	Died Later of Recurrence	Av Survival-Period of Patients who Died Later	Av Survival-Period of Patients Still Alive
Status in 1934	34	(9) 27.7%	(12) 48%	3½ yrs	5 yrs
Status in 1939	34	(9) 27.7%	(14) 56%	3¾ yrs	10 yrs

The immediate mortality in the two series of intracapsular operations (Tables II and III) is the same. In the second series of 28 intracapsular

operations (Table II) there were four late deaths, i. e. a 20 per cent mortality among the survivors. That is apparently a much better result than in the first series (Table III) in which the corresponding figure was 48 per cent mortality among the survivors five years after the initial operation, and 56 per cent ten years after. However, if we exclude in the second series (Table II) the patients operated upon in 1937 and 1938, it becomes obvious that the low late mortality is due to dilution of the material with the more recent cases, as shown in Table IV.

TABLE IV
MORTALITY STATISTICS IN 21 CASES OF INTRACANALULAR FLUCLATION
OPERATED UPON BETWEEN 1930 AND 1937

No. of Cases	Operative Mortality	Late Mortality
21	(7) 33%	(4) 28%

By excluding the recent cases the late mortality is increased from 20 per cent (Table II) to 28 per cent (Table IV), and it seems reasonable to anticipate an ever higher late mortality percentage as time goes on. Thus, in another five years, the difference between the late mortality, as given in Table II, and that represented in Table III, may decrease.

The *subtotal operations* show much better results and even if the 1937 and 1938 cases are similarly excluded, the late mortality percentage is still fairly low (Table V).

TABLE V
MORTALITY STATISTICS IN 15 CASES OF SUBTOTAL EXTIRPATIONS
OPERATED UPON BETWEEN 1930 AND 1937

No. of Cases	Operative Mortality	Late Mortality
15	(4) 27%	(1) 9%

In the group of *complete extirpations* the possibility of a recurrence is so slight that the time element need hardly be considered. This is borne out by the fact that even though the late mortality in this group is four, or 66 per cent, in only one case, or 16 per cent, could death possibly be attributed to a recurrence, though it hardly seems likely, as evidenced by the following autopsy report from the pathological Institute in Uppsala. Unfortunately the brain alone was examined.

Case No. 1058 34—A tumor, the size of a large pea, was seen compressing the floor of the fourth ventricle and lateral aspect of the medulla oblongata. Histologically, the tumor has the appearance of a young neurinoma. At the site of operation a large area of old softening with glial scar tissue is seen. Except for senile involutions no other pathologic changes were noted. (Doctor Gellerstedt)

The other three patients died from the following causes:

- (1) Cancer of the stomach, one and one-half years following the operation. No evidence of recurrence of acoustic tumor to time of death.
- (2) Parotitis, septicemia, and psychosis, four years after the operation.
- (3) Old age (74), six years after operation. No definite evidence of recurrence.

In the subtotal and intracapsular groups the late mortality was, in every instance, caused by recurrence of the tumor as far as could be determined.

In Table VI are given the deaths from recurrence with the average survival-period for each type of operation.

TABLE VI

NUMBER OF DEATHS FROM RECURRENCE IN THE THREE TYPES OF OPERATIONS

	Intracapsular Enucleations	Subtotal Extirpations	Complete Extirpations
Death from recurrence	(4) 20%	(1) 4.8%	?(1) 1.6%
Average survival-period in late deaths among recurrences	4½ yrs	4 yrs	6 yrs

The development in technical skill in performing complete extirpations, through the years, may be demonstrated by Table VII, in which the cases have been divided arbitrarily into groups of *circa* 19 each. A mortality of 11 per cent during the last two years indicated in Table VII shows the present trend, and, in the opinion of Olivecrona, a mortality of even less than 10 per cent will, in all probability, be attained in the future. In this connection it may be mentioned that no fatality has occurred among the last 16 cases operated upon with complete extirpation of the tumor.

TABLE VII

MORTALITY STATISTICS IN COMPLETE EXTIRPATIONS IN TWO YEAR INTERVALS

	Year	No. of Cases	Operative Mortality	Case Mortality	Died Later
Group I	1931-1933	1-19 (incl.)	26.3%	26.3%	1
Group II	1933-1935	20-38 (incl.)	21.1%	21.1%	1
Group III	1935-1937	39-57 (incl.)	21.1%	21.1%	2
Group IV	1937-1939	58-75 (incl.)	11.1%	11.1%	0

THE FATE OF THE FACIAL NERVE

(2) *Facial Paralysis*—The most common and obvious defect following radical removal of an acoustic tumor is a homolateral facial paralysis. This facial disfigurement, which at best can be only incompletely improved by the various plastic and anastomosing operations, is always a very unpleasant sequela to an otherwise successful operation, and may have very grave consequences for the individual. Careers have been ruined because of the presence of such a serious handicap. The hazards to which the facial nerve is exposed vary with the type of operation performed. In the *intracapsular* procedure there is much less danger of severing the nerve than in either of the two other procedures. As a matter of fact, with the present technic of having the patient's face constantly under observation during the operation, the operator always knows when he gets too near the nerve. If twitching of the face occurs, further removal of tumor in this particular region is abandoned. Thus the facial nerve may be saved in practically every instance.

In the *subtotal* procedure the facial nerve is identified in most cases after the lower pole of the tumor has been mobilized and the stalk cut at the point, and with the recent improvement in technic it is hoped that severing of the facial nerve in this group will be the exception rather than the rule.

In the *complete* procedure the danger of cutting the facial nerve is greatest. Its identification is almost always possible during the operation, but whether or not the nerve can be saved depends on the skill of the operator and anatomic conditions plus some luck.

The first attempt in this clinic* to save the facial nerve in a case of complete extirpation was made on January 4, 1937. Since then there have been 23 complete extirpations (up to June, 1939), and the facial nerve has been saved, anatomically, in 15 instances (65.2 per cent). It should be noted that all the patients in whom the nerve was saved had a complete postoperative facial paralysis except one (Case No. 271/39). The paralysis gradually diminished, usually within three months to a year. Some of the results are shown in the following photographs of patients taken at various intervals after complete extirpation of the acoustic tumor. In some of the cases in which the facial nerve had been sacrificed a Lexer plastic operation was performed, but in the majority of cases an anastomosis between the facial and the accessory nerves was carried out. The latter procedure is definitely superior to the former and was performed in a total



FIG. 5—Case 271/39. Patient three weeks after complete removal of neurinoma, with preservation of the facial nerve.

of 29 cases in the complete and subtotal groups, but never in the intracapsular group. The main effect of an anastomosis is abolition of atrophy of facial muscles and restoration of tonus. Facial movements are not restored but at least the eye can be closed by moving the shoulder.

(3) *Earning Capacity*—The ultimate aim of any operation is, of course, to return the patient to health and social usefulness. To what extent this aim has been fulfilled after each of the three types of operative procedure will be described.

First it may be stated that mere inability to obtain work has not been accepted as sufficient reason for placing the patient in the category "unable to work." The criterion used in determining a patient's inability to work has been the presence of infirmities such as poor vision, marked cerebellar disturbances, motor weakness, including that of the face, or any combination of these three, as well as total or nearly total invalidism.

The question of morbidity, then, as expressed in terms of capacity for work following each type of operation, is illustrated in Table VIII, in which,

* Previously, the facial nerve had been saved, but merely by chance, in two cases (Nos. 3278/35, 3235/33).

for the sake of completeness, the operative mortality as well as the number of late deaths are also shown

TABLE VIII

MORTALITY AND MORBIDITY STATISTICS IN THE THREE TYPES OF OPERATIONS

	No. of Cases	No of Oper- ations	Oper- ative Mortal- ity	Case Mortal- ity	Late Mortal- ity	Full Earning Capacity	Earning Capacity Dimin- ished	Unable to Work
Complete extirpations	75	75	18 7%	18 7%	6 6%	14 3%	66 1%	19 6%
Subtotal extirpations	27	29	20 1%	22 2%	4 8%	15 0%	70 0%	15 0%
Intracapsular enucleations	28	29	27 6%	28 6%	20 0%	37 5%	37 5%	25 0%

Table VIII demonstrates a fairly good showing in regard to morbidity in the intracapsular group. This is, however, largely due to the cases in which death has already occurred from recurrence. An additional factor is that some of the tumors are stationary in their growth. Doctor Olivecrona estimates that 10 to 20 per cent of acoustic neuromata remain stationary, but, unfortunately, there is no way of telling beforehand, on pathologic grounds or otherwise, just which tumor will stop growing except when it is of the cystic variety. It appears reasonable to assume, then, that in the course of time in the intracapsular group only the patients with stationary tumors will remain alive, and that among the survivors most of the patients who were not already blind before operation will have full earning capacity.

In the groups of subtotal and complete extirpations the majority of the patients have some defect limiting their capacity for work. The commonest of these defects are poor vision, facial disfigurement, cerebellar disturbances, and general weakness, less common are keratitis, sensory disturbances of the face, including tic douloureux, which occurred postoperatively in two instances, hoarseness, which persisted for several years in one case, and an occasional example of mental disturbances.

In evaluating Table VIII the longer time necessary for convalescence and reeducation following a subtotal or complete extirpation should be borne in mind, reeducation may take even as long as two years. Also, Table VIII includes early cases, in which operation was performed at a time when the technic was comparatively crude, resulting in some instances in severe cerebellar disturbances, and in two cases in a more or less complete Wallenberg syndrome. The results of increasing experience in the technic of complete extirpation are given in Table IX.

TABLE IX

MORTALITY AND MORBIDITY STATISTICS IN COMPLETE EXTIRPATION, IN INTERVALS OF TWO YEARS

Year	No of Cases	Case Mortality	Full Earning Capacity	Earning Capacity Diminished	Unable to Work
1931-1933	19	26 3%	7 7%	69 2%	23 1%
1933-1935	19	21 1%	14 3%	50 0%	35 7%
1935-1937	19	21 1%	21 4%	50 0%	28 6%
1937-1939	18	11 1%	6 3%	81 3%	12 4%

Table IX shows that during the years 1937-1939 only 12.4 per cent of the patients were completely unable to work, and this was due mainly to poor

vision, which was present prior to the operation. It is quite certain that a large number of the patients of the last two years, who at the present have diminished capacity for work, will regain, when their period of reeducation is over, full earning capacity.

In Table X a summary is given which includes a statement as to the patients' ability to walk, together with the percentage of blindness and clinical signs of recurrence. It shows that the majority of surviving patients have normal gait and station, in other words that cerebellar disturbances are not a major problem and of less significance than one might have expected.

TABLE X

A SUMMARY OF END RESULTS IN THE THREE TYPES OF OPERATIONS

	No. of Cases	Case Mor- tality	Died Later	Full Earn- ing Capac- ity	Earn- ing Capac- ity Dimin- ished	Unable to Work	Walks Nor- mally	Walks with Stuck	Unable to Walk	Blind	Clin- ical Signs of Recur- rence
Complete extirpa- tion	75	18.7%	6.6%	14.3%	66.1%	19.6%	54.4%	42.1%	3.5%	5.0%	0.0%
Subtotal extirpation	27	22.2%	4.8%	15.0%	70.0%	15.0%	65.0%	30.0%	5.0%	5.0%	10.0%
Intracapsular enu- cleation	28	28.6%	20.0%	37.5%	37.5%	25.0%	50.0%	37.5%	12.5%	10.0%	15.0%

Finally, it may be mentioned that List, in studying the capacity for work in Cushing's series of 125 followed-up survivors, found that 47, or 37.6 per cent, had full or diminished earning power. The corresponding figure in the present series of 103 followed-up survivors is 78, or 75.7 per cent, exclusive of the convalescent cases.

SUMMARY—A survey has been made of 130 cases of acoustic neuroma operated upon during the years 1930-1939. In addition, a detailed description is given of the operative technic for saving the facial nerve in cases of complete removal of the tumor. An analysis of end-results is included, with particular reference to mortality statistics, the fate of the facial nerve following operation, and the earning capacity of surviving patients.

CONCLUSIONS

(1) In this series of 130 cases of surgically verified acoustic neuroma, the youngest patient was 18 years of age and the oldest 68. The average age of the entire group is 42.3 years.

(2) Seventy-nine, or 60.8 per cent, were females, 51, or 39.2 per cent, were males.

(3) The acoustic nerve was involved in 99.2 per cent of the cases, nystagmus was present in 96.2 per cent, choked disks were found in 90.8 per cent, and roentgenograms were positive in 81.5 per cent, as evidenced by changes at the internal acoustic meatus.

(4) Improved operative technic has lowered the mortality rate to 11.1 per cent in the group of complete extirpations during 1937-1939.

(5) Complete removal of the tumor is the operation of choice when dealing with an acoustic neuroma because

- (a) Recurrences are rare
- (b) The danger of secondary hemorrhage is much less than in incomplete removal, and
- (c) The presence of scar tissue in secondary operations increases the element of danger and makes saving of the facial nerve almost impossible

(6) *Radical removal should be attempted in all cases except in those in which the tumor is cystic or the saving of the facial nerve imperative*

(7) If the saving of the facial nerve is imperative an almost complete extirpation may still be possible by leaving a bridge of tumor tissue covering the facial nerve from the internal acoustic porus to the pons

(8) The facial nerve may be saved in practically all cases of intracapsular enucleation. In the group of subtotal extirpation, improved technic has made saving of the facial nerve possible in the majority of instances. When complete extirpation was performed the facial nerve was spared in 15, or 65 per cent, of 23 cases operated upon during 1937-1939

(9) The morbidity, i.e., the degree of infirmity, as expressed in inability to work, has been lowered to 12.4 per cent in the group of complete extirpations during 1937-1939

(10) Of the 103 survivors followed-up, 78, or 75.7 per cent, had full or diminished earning power, exclusive of the convalescent cases

I wish to express my appreciation to Professor Olivecrona for the privilege of making this study

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ABDUCENS NERVE (VI) PARALYSIS FOLLOWING SPINAL ANESTHESIA

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AT THE TURN of the present century spinal anesthesia became recognized as a well-accredited procedure with such men as Bier, Fursten and Jonnesco, in Europe, and Babcock, in this country, as its staunchest supporters. Each one of these writers alluded to ocular palsies as a rare complication. Since this time, however, involvement of every one of the cranial nerves excepting the olfactory, glossopharyngeal and vagus has been reported as a postspinal complication. The abducens nerve is found to be affected in well over 90 per cent of all cranial nerve paralyses following lumbar anesthesia. Statistics, as presented by some authors, point to the incidence of paralysis of the abducens nerve as high as 1 per cent of all spinal anesthetics (Teichen¹). Cantonnet² and François³ speak of it as occurring once in every 250 cases. Why is it that during the past ten years only occasional cases are reported? It can be explained in any one of three ways. First, that our present technique and drugs have practically eradicated this rather disturbing complication, second, that these paralyses do occur but are not being recognized, and, third, that these cases do occur, are recognized, but are not being reported.

In 1906, Musham⁴ and Landow⁵ reported cases, and, in 1910, Reber,⁶ in addition to his own five cases, reviewed the literature and found 36 cases at that time. It is surprising how little has been added insofar as the pathogenesis and therapy are concerned since the early authors presented their views during the first decade of the present century. Blatt,⁷ in 1928, spoke of 87 cases, and during the same year, at the Surgical Congress in Paris, ten additional cases were reported, giving a total at that time of 97 cases in all. Since 1928, approximately 30 cases have been reported, with Dimai⁸ having the largest series, consisting of seven.

The etiology of abducens nerve paralysis is still not clearly understood. Numerous theories have been advanced by various men, with many arguments in favor of each. However, it appears that there are three general points to be considered in the pathogenesis, *viz*: (1) Frequency of paralysis of the abducens over other cranial nerves. (2) Immediate etiologic factors. (3) The rôle played by preexisting diseases.

As stated above, over 90 per cent of all cranial nerve paralyses developing after a spinal anesthetic involve the abducens. This is probably due to the fact that the abducens nerve has a long course at the base of the skull, passing around the apex of the petrosal portion of the temporal bone. The long course of this nerve, its close relationship to a bony prominence, and the extreme narrowness of the foramen through which it has to pass, make

it extremely vulnerable to environmental changes. This may explain the frequency of paralysis of the abducens nerve in such conditions as meningitis, brain tumors, and diseases of the central nervous system.

The various immediate etiologic factors that may play a part in paralysis of the abducens nerve following spinal anesthesia are as follows:

- (1) Mechanical
 - (a) Changes in pressure of the spinal fluid
 - (b) Changes in blood pressure
- (2) Toxic
 - (a) Local, direct
 - (b) Reflex
 - (c) General
- (3) Inflammatory

Those who believe the theory of mechanical causation base their arguments on such points as the fact that paralysis of the abducens nerve has occurred following ordinary spinal puncture, with no introduction of any foreign material. It is well-known that the pressure of the spinal fluid changes following spinal anesthesia. DiMaizi believes that this complication occurs in those individuals who prior to the anesthesia, have existing hypertension of the spinal fluid. The abducens nerve, already partially deprived of its reserve by the pressure to which it has been subjected, loses its ability to withstand further increase in spinal pressure following the anesthetic. He maintains that therapeutic lumbar taps definitely ameliorate the subjective complaints and clinical findings. Some individuals still believe that it is the constant leakage of spinal fluid, with resulting hypotension, that will explain the picture. Others think that the drop in blood pressure produces an anemia of the bulbar centers, with the abducens nerve being the most susceptible. The above, however, will not explain the preponderance of unilateral lesions.

In considering the toxic factor we refer essentially to the drugs used as anesthetic agents. Blatt's review listed the following drugs as being the agents responsible in a series of 97 cases of ocular palsies: Stovaine 64 per cent, novocain 26 per cent, tiopococaine 7 per cent, cocaine 3 per cent. In our cases nupercaine (1/1,500) and pontocaine (1 per cent) were the drugs employed.

Since the exact site of the pathologic process is still theoretical, the toxic action may be subdivided in the following manner: (1) Local, (2) reflex, and (3) general. By local toxic action is meant that the agent acts directly upon the nuclei or the nerves. Spielmeyer⁹ observed certain changes at post-mortem and reproduced, experimentally, in the dog and monkey the following findings: (1) Widespread lesions of the large anterior horn cells, and (2) evidence of degeneration throughout the entire length of the posterior columns as well as the posterior roots. He believed that there is a direct toxic action on the axon cylinders with subsequent secondary retrograde

degeneration of the ganglion cells. Perhaps this would explain the delayed appearance of abducens nerve paralysis. Lundy and his co-workers¹⁰ studied the changes in the spinal cord of dogs produced by a dose of procaine sufficient to cause permanent and fatal paralysis. They found peripheral degeneration of the myelin in the anterior, lateral and posterior columns of the spinal cord. This work differed from that of Spielmeyer's in that no lesions were found in the nerve roots or nerve cells.

The theory of reflex toxic action is based upon an occasional associated labyrinthine disturbance. It is thought that this manifestation could be due to a toxic absorption with subsequent reflex abducens nerve involvement.

Because of the selective action of certain agents on nerves such as (a) diphtheria toxin for the soft palate, (b) lead for the radial nerve, (c) atoxyl for the optic nerve, and (d) ergot for the posterior cord, it is believed by analogy that possibly the toxic anesthetic agent is absorbed into the general circulation and then makes its way to the specific site of action. If this is true, however, the lesions should be bilateral, and certainly should occur following subcutaneous and intramuscular injections of these agents.

The inflammatory theory infers a low-grade meningitis produced by organisms of low toxicity. Its strongest supporters give great value to cases of ocular paralysis following the introduction of air into the cerebral ventricles for encephalographic purposes.

Preexisting diseases have been condemned as definite etiologic factors. In passing we mention lues, meningitis, hypophyseal tumors, hyperthyroidism and neuropathologic states as having been accused as predisposing at some time or other.

Paralysis of the abducens nerve is usually preceded by a period of headache, dizziness, nausea, stiff neck and photophobia, following which diplopia appears. The paralysis occurs from three to 21 days after the administration of the spinal anesthetic, as shown by the following data: 3-6 days, 45 per cent, 7-10 days, 30 per cent, 11-15 days, 15 per cent, 16-21 days, 10 per cent. The diagnosis is easily made because of the restriction of outward ocular movement and uncrossed diplopia. It was at one time thought that the left nerve was more frequently involved than the right but statistics fail to substantiate this point. Women are definitely more prone to develop this complication than men. The ratio of unilateral to bilateral lesions is 3:1. The duration of the above paralysis is shown as follows: 4 weeks, 54 per cent, 5-8 weeks, 26 per cent, 9-12 weeks, 10 per cent, 3-12 months, 10 per cent. The prognosis is usually favorable, with gradual subsidence of subjective complaints and clinical findings. Blatt, however, is less optimistic and maintains that, although one may expect a "*restitutio ad integrum*," occasionally this complication may reactivate an existing neuropathologic condition which may prove fatal.

There is no specific therapy for paralysis of the abducens nerve following spinal anesthesia. The treatment is entirely palliative and usually aids in making the patient more comfortable. A spinal tap should be performed

and if the fluid is under increased pressure (manometric readings) then a sufficient amount should be removed in order to obtain a normal reading—5–15 cm of water. The paralyzed eye should be covered in order to remove the distressing diplopia. This, however, should be limited to the shortest possible time because of the fact that exclusion of the fusion tendency prevents a compensatory innervation, and aids in the development of secondary contracture. Galvanic treatment, although much employed, is helpful only as a psychotherapeutic measure. Because of the danger of injuring the retina, the current must be so weak that it does not produce a contraction even of the normal muscles of the eye. Resection and recession of the muscles should not be resorted to for a period of two years if the muscle has failed to reestablish itself.

The following is a résumé of the two cases of paralysis of the abducens nerve occurring in our hospital following spinal anesthesia.

Case 1—V. R., white, male, age 48, was admitted to the hospital, August 28, 1939, with the chief complaint of protruding hemorrhoids. Physical examination showed, in addition to the thrombosed hemorrhoidal veins, bilateral polycystic kidneys. A Mosenthal test revealed a fixed specific gravity at approximately 1.010.

Operation—September 7, 1939. Eight cc of nupercaine (1:1,500) was injected into the subarachnoid space between the second and third lumbar spaces. After waiting 30 minutes it was observed that no anesthesia was obtained, and the hemorrhoidectomy was performed after injecting novocain locally. The operative course was uneventful, the duration was 35 minutes.

Postoperative Course

First and second days. No complaints.

Third and fourth days. Patient complained of severe frontal headaches.

Fifth day. In addition to the headaches the patient first complained of double vision which was exaggerated on looking to the right side. At this time, a spinal puncture was done, and the fluid was obtained under pressure of 6 cm of water. It showed five cells per cubic millimeter. The Pandy test for globulin was negative. Examination of the fundi showed normal findings, pupils reacted to light and accommodation, no nystagmus. Paralysis of the right external rectus muscle was very obvious.

By the ninth postoperative day, the headaches had gradually subsided but it was not until the twenty-third day that the patient was free from diplopia, and at that time, occasionally, while looking off into the distance he experienced blurred vision. When the patient was discharged, on the twenty-fourth postoperative day, paralysis of the abducens nerve had entirely disappeared. A three-month follow-up revealed the patient free of symptoms.

Case 2—W. B., white, male, age 17, was admitted to the hospital, September 5, 1939, with an undescended right testicle. Temperature 98.6° F, pulse 90, respirations 20, blood pressure 130/90. Physical examination was entirely negative other than that the right testicle was found in the inguinal canal.

Operation—September 11, 1939. A first-stage Torek was performed under spinal anesthesia. Pontocaine (1 per cent solution), 12 cc plus 12 cc of spinal fluid, was injected between the third and fourth lumbar vertebrae. The anesthesia was entirely satisfactory, with the height obtained being equivalent to the level of the tenth dorsal nerves. The duration of operation was 60 minutes. The anesthetic course was uneventful.

Postoperative Course

First and second days Uneventful

Third to fifth days Intermittent headaches

Sixth day Patient complained of diplopia, particularly on looking to the right. Spinal puncture revealed the pressure to be apparently normal (no manometric reading). Cytologic examination revealed two cells per cubic millimeter. The Pandy test was negative. Physical examination showed normal fundi and visual fields. The left pupil was slightly larger than the right and both reacted well to light and accommodation. Paralysis of the right external rectus muscle was present.

The headaches disappeared by the seventh day, the diplopia persisted but gradually became less pronounced. At time of discharge (twenty-first day) the patient complained of diplopia only when looking far into the distance.

An interesting point in the first case is that no anesthesia was obtained and yet paralysis of the abducens nerve ensued. What may be deduced from this observation? It certainly points against the theory of a direct toxic action. With the absence of fever, with the presence of negative cytologic findings, and with the blood counts normal, the theory of low grade inflammation as a causative factor seems remote. It is our contention that paralysis of the abducens nerve following spinal anesthesia is due to a disturbance in dynamics of the spinal fluid. The mechanics of this reaction are still unknown.

SUMMARY AND CONCLUSION

The clinical aspect of paralysis of the abducens nerve complicating spinal anesthesia is discussed. Two cases are presented.

The etiology of the complication is still unknown, however, we believe that the problem will be solved on the basis of a disturbance in the dynamics of the spinal fluid during spinal anesthesia.

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THE DEFORMED CHIN AND LOWER JAW

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THE SOCIAL ASPECTS of plastic surgery are of wide implication, and have been reviewed by the author¹ elsewhere. Suffice it to say that a deformed chin and lower jaw are most detrimental to one's appearance, and frequently such stigmata cause an inferiority complex in the individuals so afflicted, and they refuse to lead a normal social life. These unfortunates and the public have erroneously heard that a receding chin denotes weakness of character. The layman believes, therefore, that the dimensions of the chin give the face a characteristic expression of weakness or strength.

Plastic repair of the deformed nose has become an important and gratifying procedure. Its progress has been responsible for the demand and necessity for the correction of other facial feature defects to make them harmonize with the nasal repair and thus to create profile harmony. In cases of a combined large nose and receding chin (Figs. 5 and 6), much can be accomplished by the removal of the nasal hump followed by the transplantation of the hump over the front of the mandible.

The object of this paper is to evaluate the methods in use at present for the correction of chin and lower jaw deformities, and to show what we may expect from the surgical correction thereof. We shall not consider operative procedures that have been discarded, but only those which, after long experience, have proved their value. It behooves the surgeon to develop one method and to perfect his technique rather than to use several methods with confusion and poor results. This presentation does not include conditions arising from burn cicatrices, loss of substance, and disease, as the reparative surgery of such would involve a separate lengthy dissertation. In any plastic procedure, we strive toward a double goal. It is axiomatic to have functional adequacy and esthetic perfection. In the topic under discussion these two are complementary, because we cannot have perfect facial contour unless the teeth and mandible are faultless in occlusion.² Any degree of protrusion or retrusion of the mandible will affect the facial contour. The function of the mandible depends upon its contact with the superior maxilla. In other words, the teeth of the maxilla and the mandible must properly occlude. In prognathism, the lower jaw is too far forward, and is usually accompanied by underdevelopment of the superior maxilla. In mandibular recession, or retrusion, the lower jaw is too far backward. Uneven development of the sides of the mandible produces lateral asymmetry and imperfect lateral occlusion. The individual so affected has a tremendous functional disability, so far as mastication is concerned.³ The use of prosthesis and orthodontics are satisfactory in only the minor deformities. The orthodontist is only successful, at best, when he is able to begin treatment early in life. Since mandibular deformities are progressive during the period of development, they

should be treated as soon as the permanent teeth erupt. In most cases where the orthodontist has improved function, the residual chin recession usually persists and necessitates plastic repair.

RECONSTRUCTION PROGRAM—There are three distinct periods or phases of jaw reconstruction. The preoperative period, the operation itself, and the postoperative treatment. In the first phase, it is necessary to rule out any existing infection or systemic disease. Also, during this phase, plaster casts are made of the upper and lower teeth, as this is an aid in computing the occlusion after section of the bone. Roentgenograms are made (1) to determine the condition of the teeth which are to hold the splints for postoperative fixation, (2) to show any infected area, and (3) to visualize the location of the mandibular foramen, injury to which must be avoided in order to preserve the blood and nerve supply of the teeth. As a matter of record and as an aid in preparing the case, photographs are taken depicting the face from all angles. In cases of retruded chin, a plaster cast of the face is made on to which modeling clay may be added to determine the amount the chin is to be brought forward. Thus, the size and shape of the transplant to be used is calibrated. The technic of the operation itself is explained subsequently, and the postoperative treatment will be described under the topic treating each deformity.

Local anesthesia (2 per cent) novocain with 15 drops of 1-1000 adrenalin solution to the ounce) is used almost exclusively. It is obtained by blocking the mandibular division of the trifacial nerve and by supplementary local infiltration of the area. In addition to the external infiltrations, anesthesia of the inferior alveolar nerve is obtained by intra-oral block. General anesthesia, when used, is given via the nose through an endotracheal tube. Preoperative sedation is accomplished with a substantial dose of a barbiturate (4 gr. of sodium pentobarbital) given one and one-half hours prior to the operation. If the patient is not sufficiently composed 30 minutes before the operation, a narcotic is given (morphine sulphate 1/6 gr. with hyoscine 1/150 gr.). The use of narcotics is to be avoided as it frequently causes vomiting, and thus disruption of the postoperative fixation of the jaws.

PROGNATHISM—Prognathism (Figs 1 and 2) is a deformity of the lower jaw characterized by an abnormal protrusion of the mandible.⁴ In this condition, the lower incisors are 1 to 3 cm. in advance of the upper incisors, and the lower teeth do not occlude with the upper teeth. In addition to the unsightly appearance of the patient, the masticating powers are completely crippled. Phonation is impaired because the cheeks and lips are unable to properly function. This condition is most often accompanied by underdevelopment of the maxilla. This underdevelopment of the maxilla is due to the tongue finding excessive room in the lower dental arch and thus it does not exert adequate pressure upon the upper arch (maxilla) to promote its full development. It is interesting to report the observation that in cases of prognathism the tongue undergoes a compensatory hypertrophy which subsides to normal after surgical correction of the jaw. The author prefers

to increase the efficiency of the jaws by osteotomy through the ramus of the mandible to lengthen the jaw when retruded, and to shorten the jaw by a similar procedure when prognathic. Too much emphasis cannot be made upon the importance of avoiding injury to the inferior alveolar nerve and vessels.



FIG. 1—Prognathic jaw Before operation



FIG. 2—Prognathic jaw After operation (Nasal plastic operation performed two weeks previous to jaw operation)

Etiology—Mandibular deformities are attributed to the following factors: (1) Any condition which hinders the contour of the mandible during the growth period, such as ankylosis of the temporomandibular joint, (2) cleft lip and palate, (3) thumb sucking, (4) constitutional disorders, such as rickets, syphilis, *etc.*, (5) endocrine disturbances such as acromegaly and cretinism, and (6) traumatism and infections, such as ununited fractures of the lower jaw, osteomyelitis, and contracting scars.

Dental consultation is of paramount importance in the correction of the mandibular deformities. The dentist must prepare the mouth for the operation, construct casts, and aid in devising the splints for fixation of the jaw in its new position. Following surgical correction, the dentist frequently aids the occlusion by orthodontic procedures. A combination of surgical correction and orthodontic treatment usually produces the best end-results. There are several classifications of mandibular deviations and the character of the bony deformity varies greatly. The classification is of relatively little value as in practically all cases the treatment is the same.

Treatment—The treatment consists of an amalgamation of orthodontic, surgical, and sometimes prosthetic measures. Orthodontic measures attempt to improve the occlusion and correct facial asymmetry by subjecting the teeth to pressure. This pressure is, in turn, transmitted to the bony structures in a fashion which will force the teeth into a normal occlusion. By this method

the orthodontist endeavors to reshape the jaw. This is usually attempted by means of wire splints and rubber bands. These methods serve their best purpose in young individuals before puberty. Soon after this time the bone is no longer pliable and only surgical treatment will produce the necessary physiologic and esthetic effect. Since a retruded or prognathic chin is of progressive severity during the developmental period of the jaws, the sooner it is treated the better. Many of these operative procedures can be obviated if the defective articulation is observed early and appropriate orthodontic measures started as soon as the permanent teeth erupt.

Surgical Treatment—The choice of a method of surgical treatment is by (1) osteotomy or (2) ostectomy.

Osteotomy (Plate A) is employed by dividing the ramus of the mandible followed by shifting of the body of the bone backward to the desired position, after which immobilization is maintained until ossification of the bone is complete. This is the most satisfactory of the operative procedures because it is simple in conception, entails no sacrifice of the bone, no injury to its blood and nerve supply, does not damage the mandibular arch and its teeth, obviates opening into the oral cavity, and reduces to a minimum the muscle traction which tends to obstruct the reduction. There are some dangers to this method. They are injury to the parotid gland, facial nerve, and internal maxillary artery. However, with ordinary care, practice and skill, these dangers are negligible.

The optimum site for the bone incision employed in this method is through the ascending ramus of the mandible in the area between the mandibular notch and the mandibular foramen. This is the safe area (Plate A, 3 b) and is above the entrance of the inferior alveolar nerve and vessels into the mandibular canal. Before the operation is started, the safe area is visualized roentgenologically. After the section of the ascending ramus, there is a tendency on the part of the upper fragment to become displaced by the temporal and external pterygoid muscles. When this does occur it would lead one to believe there would result a permanent closed or open bite. However, this is not the case, as the callus formation in this area is of sufficient strength to result in excellent function even where there is slight contact of the fragment edges (Plate A, 5 b). By this method the nerve and blood supply to the teeth are uninterrupted and the resultant function is normal.

Other operators have described various locations at which to perform the osteotomy, such as section of the bone at the mandibular angles. At this site, the technic of the operation is simplified, but the blood and nerve supply is severed. Although good esthetic results have been reported, it is the author's experience that there is an unnecessary damage to the blood and nerve supply resulting in trophic disturbances of the teeth and loss of sensation anterior to the osteotomy. This and other methods are only mentioned to be condemned and, therefore, a description of these methods is purposely omitted. The technic used with great success is as follows.

Procedure (Plate A)—A stab wound is made at a predetermined site

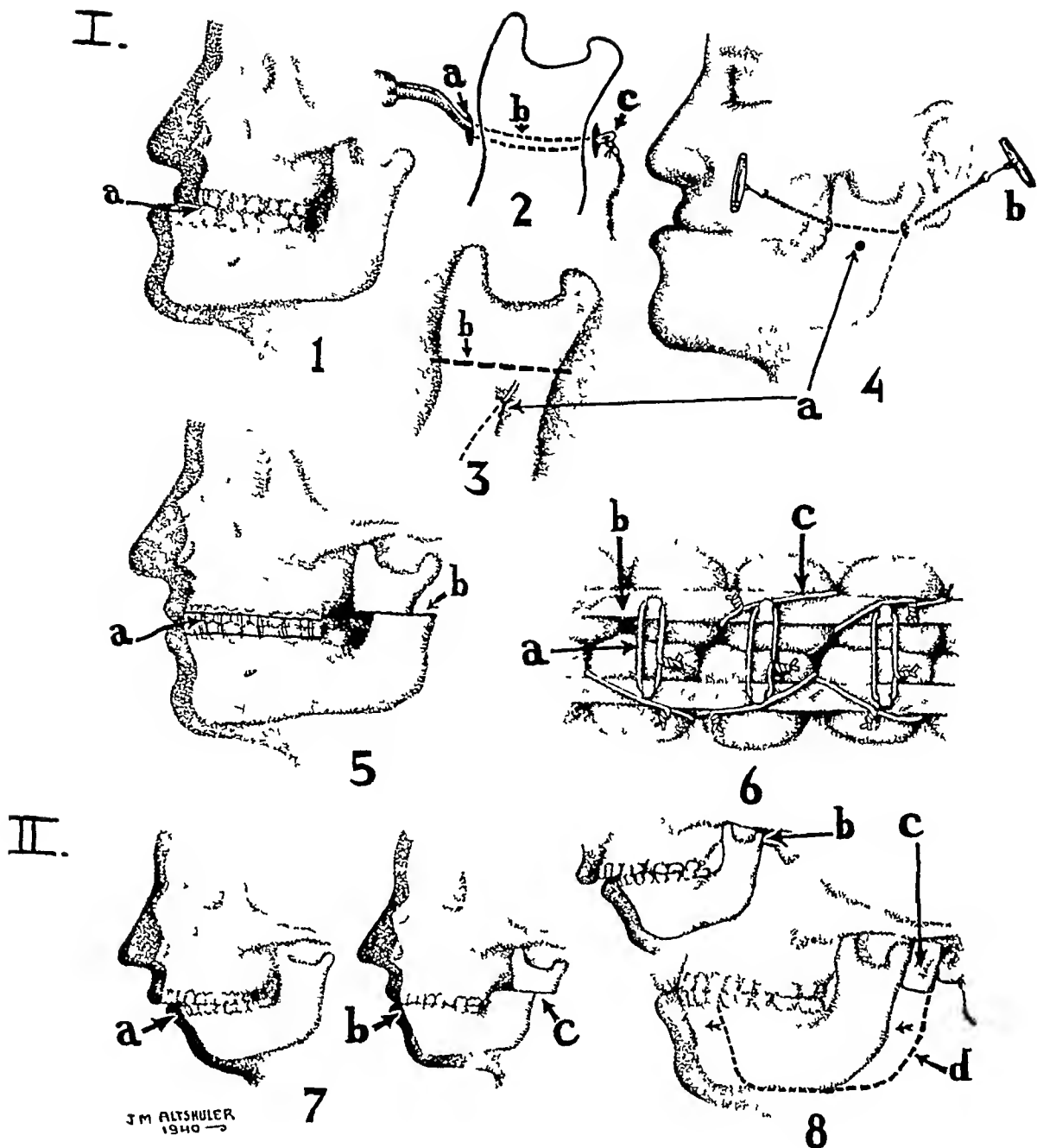


PLATE A
I SURGICAL CORRECTION OF THE PROGNATHIC JAW

- (1) Deformity
 - (a) Lack of occlusion between upper and lower incisor teeth
- (2)
 - (a) Stab wound
 - (b) Pedicle needle passed behind ramus, hugging the bone closely so as to avoid penetration of oral mucous membrane
 - (c) Stab wound at point of emergence of pedicle needle and attachment of Gigli saw to pedicle needle
- (3) Internal view of ramus showing operative field
 - (a) Site of entrance of inferior alveolar nerve and vessels
 - (b) Site of proposed bone incision in "safe" area
- (4)
 - (a) Site of entrance of inferior alveolar nerve and vessels
 - (b) Gigli saw in proper position for osteotomy
- (5) Deformity corrected
 - (a) Splints for immobilization of fragments after repositioning of bone
 - (b) Distance lower jaw is brought backward
- (6) Retention splints used for immobilization shown in detail
 - (a) Wires passed between lugs on arch bars
 - (b) Arch bars for upper and lower jaw
 - (c) Method of passing wires around arch bars anchoring them to teeth
- II SURGICAL CORRECTION OF THE RETRUSION OF THE LOWER JAW, WITHOUT NORMAL BITE
- (7)
 - (a) Degree of retrusion showing malocclusion of teeth
 - (b) Advancement of jaw correcting bite
 - (c) Distance lower jaw is advanced
- (8) Alternate method of surgical correction (Babeock)
 - (b) Site for cartilage implant
 - (c) Quadrilateral section of rib cartilage inserted between condyle of mandible and bony acoustic meatus
 - (d) Resultant amount of lower jaw advancement

approximately 2.5 cm above and behind the angle of the mandible. A specially prepared curved pedicle needle is introduced, hugging the bone as close as possible on the inner surface of the ramus of the mandible. (This needle forms nearly a half circle, 4 cm in diameter.) The point of the needle emerges by way of a stab wound at the anterior border of the ramus of the mandible. A heavy silk suture is passed through the eye of the needle and this pilots a Gigli saw into position (Plate A, 2). In this area the ascending ramus is sectioned horizontally between the mandibular foramen and the mandibular notch (Plate A, 3 and 4). The same technic is carried out on the opposite ramus. After this, it is possible to push back the body of the mandible until the desired occlusion of the teeth is reached (Plate A, 5). The upper and lower teeth are then fixed in proper occlusion with suitable splints and wire ligatures. There are many types of retention splints used but the one shown on the accompanying Plate has been found most satisfactory by the author (Plate A, 6). These splints are attached to the teeth the day preceding the operation and are wired together immediately following the operation. Single arch-bars containing lugs are attached, one to the upper and one to the lower teeth, by means of wires passed around the teeth. Wires are then passed between the lugs on the arch-bars, holding the jaws immobilized. The jaws are thus retained in position with these wires for ten weeks, after which time union of the fractures has taken place and normal function of the jaw is imminent. It is necessary to tighten the wires at weekly intervals so as to insure complete immobility during the healing period.

This apparatus, used for immobilizing the jaws, is kept on longer than necessary (usually ten weeks) so as to avoid refractures that would follow early removal and use of the jaw. Roentgenograms aid in visualizing the amount of ossification present. The best indication, however, is the decreasing amount of tenderness over the site of the bone incision. After the splints have been discarded, there is some limitation of motion because of the prolonged period of fixation. This stiffness disappears after a few days of progressive mastication. Physiotherapy and massage are aids.

Postoperative Treatment—Antiseptic sprays, mouth washes, and frequent brushing of the teeth is advised. The diet consists primarily of liquids with some semisolids. It should contain sufficient caloric value to maintain the patient's normal weight and at the same time avoid constipation. The average adult, weighing 70 Kg, requires a diet of 2,500 to 3,000 calories daily. A variety of food and liquids, well cooked and properly flavored and seasoned to tempt the appetite, are prescribed. Meats prepared with a grinder are taken easily and a large amount of food is sucked between the teeth without any difficulty. Many adequate diets consisting of milk drinks, fruit juices, pureed vegetables, *etc*, have been described.⁵ If for any reason the food cannot be drawn in, it can easily be sucked through a rubber tube, passed behind the last molar tooth or through any empty socket, if present.

In the rare case where these methods are not applicable, a soft, well-greased catheter is passed into the pharynx.

Osteotomy is an open operation and consists of the removal of a section of bone from both sides of the horizontal ramus of the mandible and the repositioning of the bone backward into the space thus created so that the teeth will fall into normal occlusion.

An incision is made under the horizontal ramus, the periosteum is elevated and the bone is resected according to a previously prepared pattern. This can be done with a Gigli saw or a chisel. The bone fragments are immobilized by previously constructed splints and also by wiring the detached portions, which may ultimately necessitate an additional operative procedure for the removal of this wire.

This method, which is advocated by some surgeons, has additional disadvantages and the author advises against its use for the following reasons: (1) If the jaw is not edentulous at a convenient location, teeth have to be extracted in order to make room for the excision of bone. Thereafter, sufficient time must be allowed for healing. The extraction is usually done five to six weeks before the operation, (2) there is considerable scarring due to the external incisions when this method is used, and (3) the danger of infection is increased, due to oral contamination sometimes resulting in osteomyelitis.

RETRUSION OF THE LOWER JAW WITH NORMAL BITE—This group includes microgenia which is entirely an esthetic defect. This condition is due either to underdevelopment of the front of the mandible (mentum) or a defect in the fatty cushion covering this area. The repair demands the addition of a transplant to bring the chin forward the required distance. Various types of implants have been used for this purpose, such as ivory, iliac bone, fat, and dermal grafts, and prosthesis. Only two materials which have proven satisfactory in the greatest majority of cases will be described. One is the osteocartilaginous nasal hump, which may be removed from the nose when it accompanies a slight chin recession (Figs 5 and 6). It is easily obtained by endonasal rhinoplasty. After removing the periosteum and nasal mucosa, the hump is inserted in the chin as shown in Plate B. The author has also successfully transplanted such a nasal hump from one individual to the saddle nose of another, proving its adaptability in many locations as a graft. When there is no accompanying nasal hump available for the chin, refrigerated human cartilage is used (Figs 3 and 4). This makes the ideal transplant material for all surface defects. This cartilage is easily acquired from autopsies of nonpathologic specimens, especially accident-death cases.

The cartilage is denuded of its perichondrium and refrigerated in a solution of aqueous merthiolate one part to four parts of sterile normal saline.⁶ It may be stored indefinitely. The solution is changed every four weeks, and each time before use a culture of the solution is taken. The author is yet to obtain a positive growth from this solution. This cartilage can be transplanted regardless of age, sex, or color. Its use is restricted until it has been



FIG 3—Retrusion of lower jaw with normal bite Before operation



FIG 4—After operation—Retrusion of lower jaw repaired with modeled refrigerated human cartilage graft (Nasal plastic performed at same operation)



FIG 5—Combined nose and chin deformity Before operation



FIG 6—After operation (Retrusion of chin corrected with "hump" from nose obtained by endonasal rhinoplasty at same operation)

refrigerated at least one week. A few of its many advantages are (1) It is easy to obtain, (2) it does not curl, (3) it can be made sterile, (4) it obviates the necessity of a chest operation for rib cartilage and the complications thereof, such as scars, opening into the pleura, *etc.*, and (5) it is readily retained and assimilated by the tissues. It will be difficult to find a substitute for refrigerated human cartilage that will "take" as an implant in so high a percentage of cases, require removal so infrequently, and leave so satisfactory and enduring an esthetic effect.

The operative technique shown in Plate B is as follows. The skin is prepared with tinctures of green soap and metaphen, and a submental incision is made in the natural skin fold. A pocket, slightly larger than the size of the implant, is prepared with a comma-shaped knife carried down to the periosteum which is scarified to aid adherence of the implant. One end of the previously prepared transplant is inserted with bone forceps as far laterally as possible. A small two pronged pointed retractor is then inserted into the opposite end of the incision, which readily stretches until the protruding end of the graft can be brought into the pocket. The incision is then closed with a single suture of horse hair, and is covered with a strip of 5 per cent xeroform ointment gauze, over which is placed one layer of dry gauze, with a firm elastoplast dressing. This is assurance against misplacement of the graft and the formation of hematomata, either of which may cause failure.

Postoperative treatment is simple, as the patient has no discomfort. The diet consists of fluids for 24 hours and thereafter, as an aid in the immobilization of the graft, a soft diet is prescribed to avoid chewing. On the fourth day, the first dressing is done and the single suture removed. Another snug dressing is applied for three days until, at the end of the week, all bandages are removed. The incision rapidly becomes invisible.

RETUSION OF THE LOWER JAW WITHOUT NORMAL BITE—To correct this condition it is necessary to elongate the mandible. The chin and lower incisor teeth are far behind the normal position (Plate A, 7 a), thus, this condition is the antithesis of prognathism. Many methods of correction have been utilized with varying degrees of success, such as the method illustrated in Plate A, 8 b, c and d, where a block of cartilage is inserted between the mandibular condyle and the bony acoustic meatus. This advances the lower jaw the distance corresponding to the thickness of the cartilage graft, thus overcoming the retusion.⁷ The correction, however, is best obtained by exactly the same operative procedure as described above for the correction of prognathism. The operative technique, fixation of the jaws, and post-operative care are the same as described for prognathism. The horizontal sections (osteotomy) are made through each ascending ramus of the mandible, and are shown on Plate A, 4, permitting the advancement of the lower jaw to a forward position, as seen in Plate A, 7 b and c. The jaws are immobilized by means of splints attached to the teeth by the same method above described for prognathism (Plate A, 6). If this advancement of the lower jaw is not

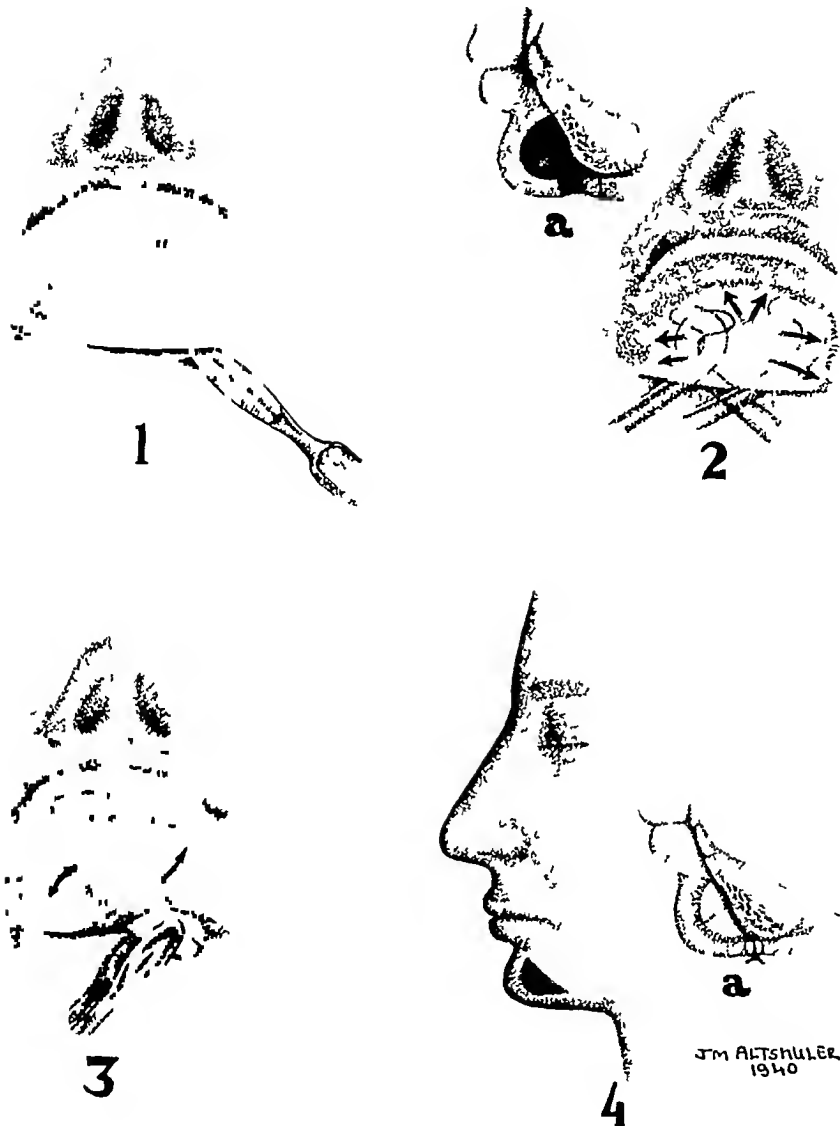


PLATE B
CORRECTION OF RECEDING CHIN

Unassociated with Malocclusion by Utilizing Modeled Refrigerated Human Cartilage Graft or Nasal Hump

- (1) Submental incision in skin crease
- (2) Formation of pocket for implant
 - (a) Sagittal view of prepared bed for implant
- (3) Introduction of implant
- (4) Implant *in situ*
 - (a) Sagittal view showing implant *in situ* with skin suture

sufficient to overcome the retrusion, it may be supplemented by the addition of a refrigerated cartilage graft which will give further prominence to the chin, as shown in Plate B

SUMMARY AND CONCLUSIONS

Deformities of the chin and lower jaw have a social and esthetic effect and, when accompanied by faulty occlusion of the teeth, there is a concurrent functional disability

The correction by orthodontics is possible only when attempted early in life

The three phases of jaw reconstruction are described

The method of choice for the surgical correction of prognathism is osteotomy. The ramus of the mandible is sectioned at a predetermined site, in the "safe area" to avoid interruption of the blood and nerve supply, and the body of the mandible is pushed back into the desired position

The postoperative fixation of the jaws is maintained by approximate interdental splints and wire ligatures

Retrusion of the lower jaw, when accompanied by a normal bite, is best corrected by the addition of the osteocartilaginous hump obtained by endonasal rhinoplasty. When there is no accompanying nasal hump, refrigerated human cartilage is used

Retrusion of the lower jaw without normal bite is corrected by the same method described for the correction of prognathism except that the lower jaw is moved forward to the desired position

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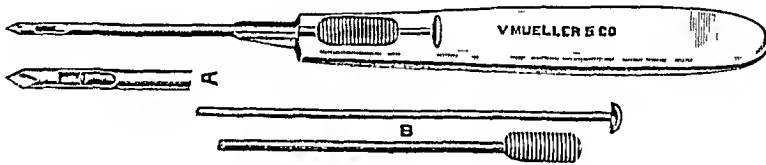
AN IMPROVED BIOPSY PUNCH

M L WEINSTEIN, M D , M SCHINDLER, M D ,
AND E LAWRENCE ADAMS, M D

CHICAGO, ILL

FROM THE SURGICAL DEPARTMENT OF THE CHICAGO MEMORIAL HOSPITAL CHICAGO, ILL

THIS PUNCH* consists of three parts. A combined trocar and cannula (A), a No 18-gauge cutting cylinder (B), and an obturator (Fig 1). The mass for biopsy is perforated by the trocar and cannula, and within the latter the cutting cylinder is slid up and down, nipping off the desired tissue. The cylinder may then be removed and emptied of tissue by means of the obturator—leaving the combined trocar and cannula *in situ*. If the mass is cystic, fluid may escape through the cannula and its nature may be studied.



This instrument has proven useful for biopsy diagnosis in cases accessible for puncture, as in breast tumors, sarcomata of the extremities, lymph nodes, etc. It has been found particularly useful when the patient refuses incisional biopsy. The instrument has the added advantage of making a single puncture and taking as much tissue as may be required without reintroducing the trocar. In suspected malignancy, a coagulating current may be applied to the instrument or a fulgurating wire inserted through the cannula before the instrument is removed. In this way hemostasis and the spread of malignant cells may be controlled.

* The instrument is manufactured by V. Mueller Company, Chicago, Ill.

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The Annals of Surgery in Spanish

WITH the simultaneous publication of this June Number of the Annals of Surgery in Buenos Aires, Argentina, by the Guillermo Kraft Company, and in Philadelphia by J B Lippincott Company, the journal and these two venerable publishers enter upon a new epoch in their long careers

No better symbolic demonstration can be given of our sincere willingness for a permanent intellectual fraternization between the surgeons of North and South America

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The Annals of Surgery was founded by Dr Lewis Stephen Pilcher, in 1885, to meet what he thought was the need for the first journal of its kind in the English language. It was not until the 26th Volume appeared, in July, 1897, that J B Lippincott Company took over its publication and continued its successful development

The Annals began to publish the Proceedings of the New York Surgical Society in 1885, and of the Philadelphia Academy of Surgery in 1893. It became the official organ of the American Surgical Association in 1928, although since the foundation of this Association in 1880 it has published the large majority of the papers presented before it. Since 1935 it has been the official organ of the Southern Surgical Association

In addition to the manuscripts received from these national surgical associations, the pages of the Journal have been in the past, and are at the present time, open to the publication of original contributions, controversial and original surgical subjects, and surgical research

The policy of the journal has been formulated by a distinguished editorial board representing the medical schools and the national surgical societies of the United States and Canada. In the future this board will sincerely hope to secure the support, inspiration and privilege of consulting members from our sister republics in South America, where surgical work of such a high caliber is being performed.

In the past the journal was published only in English, in spite of the fact that it has been distributed in 35 foreign countries. Beginning with this issue it will be published in Spanish and will be distributed by the Guillermo Kraft Company. Thus wrapped in the fine raiment of the language of the immortal Cervantes, our new journal will be able to enter the hospitals and consulting rooms of Latin America as an intimate friend and surgical coworker. It will enlarge its usefulness, and bring to North Americans the advantage and privilege of a genuine understanding of feelings and ideas that only language clearly expressed can convey. To us in North America this free intercourse of ideas and feelings with our surgical colleagues of South America is an inestimable advantage from which we have been too long deprived. To our mutual good fortune, this joint enterprise of the *Annals of Surgery*, the Guillermo Kraft Company, and the J. B. Lippincott Company has turned to reality what for some time seemed only a dream difficult to attain.

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Chairman Editorial Board

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APRIL 6-8, 1942

ADDRESS OF THE PRESIDENT

THE DEFENSE OF THE HUMAN BODY AGAINST LIVING MAMMALIAN CELLS*

HARVEY B. STONE, M.D.

BALTIMORE, MD

EVERY LIVING ORGANISM depends for its survival on the possession of at least two powers. The power of adaptation and, if necessary, resistance to its external environment, and the power of maintaining stability, within certain limits, of its own internal economy. These two abilities are found in all animals from ameba to man, but apparently the problems involved grow in complexity with the increasing complexity of structure and function of the higher forms of life. This is well illustrated by the response to trauma. The cutting in half of certain of the simpler living creatures may result in each half forming a complete new survivor. Such mechanical insult to any of the adult higher animals would be invariably fatal, but note that the earliest stage of the fertilized ovum, even of man, can also apparently survive complete fission. But the response to trauma is only one of many reactions of defense against the external environment. Another great field of reaction is dependent upon the intimate presence of other living organisms or their products, and includes within its scope such conditions as infection, parasitism and intoxications. In the higher animals, and particularly in man, the psychic or emotional reaction to the environment is another manifestation of response of the greatest interest and importance. Now much fruitful study has been devoted to these and other particular forms of response-behavior in many different animals, and while, no doubt, much remains to be learned, at least the problems have been recognized, methods of attack have been devised, and many substantial results have been obtained. As much cannot be said for our knowledge of the defense mechanism against the introduction of alien living mammalian cells.

The second great power of the organism, that of regulating and controlling its internal functions, also, has many specific phases that have been the subject

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of long and intense study. Digestion, absorption, secretion, the maintenance of the circulation, the function of the nervous system, are but partial aspects of the subject that we have called general physiology. Physiology, in its classical sense, does not cover the whole field. The physical and chemical processes that regulate and maintain the composition and osmotic pressure of body fluids, the phenomena related to membranes, surfaces and molecular behavior fall within the scope of biochemistry and biophysics. The conscious and subconscious states that affect the internal activities of the body are material for the student of psychology. All of these varied and numerous functions must be coordinated and equitably controlled if the higher animal, particularly man, is to survive and prosper. To this regulated interrelationship Cannon¹ has given the name "homeostasis." His numerous writings on the subject have greatly helped to establish and popularize this concept of the living being as a mechanism dependent upon a highly complex system of internal checks and balances. Here again, a vast deal has been learned and much still remains to be learned. At any rate, methods and techniques of study, many of them intricate and highly specialized, have been evolved and successfully applied.

There is a special phase of this whole problem that has apparently lagged behind, at least so far as the interest of the medical profession and of surgeons is concerned. To be sure, the biologists have engaged themselves with it, but often the living material with which they work is so different from the human, that their results may not be transferable. I refer to the reaction of the higher animals, particularly man, to the living cells of mammals. The problem has two distinct aspects that correspond to the two properties of living creatures just now set forth, and each of them is rich in theoretical and possibly practical interest. The first concerns the reaction of human beings to implanted living mammalian cells—a defense reaction. The second concerns the control of the human being over the growth, destruction and repair of its own cells—a special phase of homeostasis. Later, a development of these two statements will be attempted. Perhaps here it may be well to glance briefly at some of the biological studies bearing on the problem.

Dr. Ross G. Harrison² has employed heteroplastic grafting extensively in his experimental studies of embryology. By this technique he has made many fundamental contributions to his chosen field, particularly the cystologic sources and relationships in the development of many structures. What concerns us here is the remarkable success of some of these grafting experiments. In the amphibia during the larval stage, not only may organs such as the eye, and whole limbs, but, indeed, large parts of one animal may be successfully grafted onto another animal. These grafts will take between individuals of different species, and some of such composite animals, called chimeras, have developed through the stage of metamorphosis into living adult forms. This tolerance for foreign tissues does not exist in the same degree, of course, for the higher animals among the vertebrates, in which respect there is a graded series, the higher forms showing increasing resistance to such alien

grafts It has been stated that successful cross-grafts between species are limited to cold-blooded animals, and that in mammals even grafting between individuals of the same species and variety encounters great intolerance except in cases of close blood relationship

That these statements are not universally true is evidenced by the work of Eastlick,³ who transplanted limbs between embryos of various avian species with a certain number of successful experiments that survived hatching and lived with the foreign limb also surviving We are fortunate in having on our program to-day Doctor Willier, whose intensely interesting original work is in the same general field Leo Loeb⁴ has done a great deal of interesting work upon the general subject of transplantation and, in 1930, published an extensive review of it In this he records observations of many writers, in addition to his own investigations, and presents a philosophical discussion of the whole problem He introduces a special terminology, using the expression "organism differential" to indicate the basic differences between different animals and "individuality differential" to mean the total of physical and chemical characteristics peculiar to the separate individuals of the higher animal series These he attributes to the specific genes and chromosomes Except perhaps for identical twins, no two higher animals are exactly alike in these endowments There is a graded scale of increasing diversity beginning with siblings, extending through blood relatives, variety, species and genera Because of this inherent endowment an individual possesses a chemical constitution to which cells from any other source are alien in varying degrees, and in which they provoke a reaction that leads to their destruction He does not believe that this inherent reaction can be modified or broken down by any method yet suggested

There has been, of course, an enormous amount of clinical work done on the general subject of grafting, and a great deal on cross-grafting Most of this has been confined to the reporting of the introduction of various tissues into human beings, with an overwhelming incidence of failure, but without serious effort to explain or prevent the failure Among the few publications that deal with underlying conditions affecting cross-grafts is Holman's⁵ work on protein sensitization in isoskin grafting Holman doubts that cross-grafts of human skin are ever successful, finds that taking grafts from donors of the same blood group as the host makes little difference in the generally poor results, and attributes these results to the chemical differences between the tissues of host and graft He thinks the grafts serve as sources of foreign protein intoxication, and lead to the development of a reaction like anaphylaxis He further cites observations that suggest that this reaction is highly specific against the donor tissue causing it, and does not affect grafts from another donor, which, however, soon develop their own specific destructive chemical reaction

The control of the multicellular animal over its own cells is obviously an instance of the general principle of homeostasis However, it has received far less consideration, or, at least, efforts to study it have been far less successful

than in the case of other mechanisms of homeostasis. The movements of water, salts and proteins between the blood, the lymph, the intercellular spaces, and the cells themselves have been the subject of much study and impressive results. But who knows why the thyroid gland reaches an optimum size and then stops growing? Why do certain tissues throughout life possess the power of regeneration after injury, and other tissues have this power only in a very limited way, or only in embryonic life? What stops the regeneration of tissues when they reach the optimum stage, and prevents abnormal overgrowth? There are many such questions that we have all asked ourselves many times. They lie at the root of this problem of cellular homeostasis. The investigative attack on them has so far been very unproductive. We take refuge in speculative phraseology. We say an organ's size is conditioned by the physiologic need for it. But what mechanism implements that need, and what brakes keep it in check? Is it a balancing of hormonal stimulants? Is tissue pressure a factor? Does the metabolic product of a certain type of cell exert an inhibitory effect upon the growth of that type of cell? These things should be susceptible of investigation, if we can evolve proper technic. This matter of normal balance and restraint of cells and organs has its highly practical importance as well as its biologic interest. It concerns the healing of every wound, the response of work hypertrophy on the muscles, the development of compensations for damages done to various structures. It also, of course, is fundamental to the whole cancer problem. Every pathologic new growth represents an escape of a special tissue from the general restraints of cellular homeostasis. A great deal of study has been devoted to the discovery of carcinogenic agencies, and most valuable progress has resulted. Less attention has been given the defense mechanism against cellular overgrowth. Perhaps the problem is much harder to grapple with. At the present time, one might generalize the situation somewhat as follows. A normal cell is subject to the normal restraints on its growth and reproduction. A greatly abnormal cell, badly damaged or perverted greatly in its internal mechanism, becomes essentially a foreign cell, and hence the victim of the normal defense reaction against alien cells and is thrown off or destroyed. But a cell somewhat modified from normal by some agency—chemical action, radiation effect, or what-not—may be near enough to normal to escape the destructive reaction against alien cells, yet sufficiently diverted from normal to escape the restraining mechanism of normal cellular homeostasis. That is cancer. Should we not then concern ourselves more with these two great basic protective mechanisms which perhaps are really different phases of the same mechanism and try to discover how they work? We may learn how to sharpen the body's discrimination against damaged cells, in other words, heighten its cancer resistance, if we know the method of discrimination against alien cells. It is helpful, no doubt, to state a problem, but far more difficult to solve it, and, so far, no very promising line of attack has been developed in the study of the mechanism of cellular homeostasis. Perhaps the approach may be less arduous to an understanding of the defense of the body against alien mammalian cells.

That the human body does possess such a defense mechanism against

these cells will be generally admitted. All the evidence of clinical medicine and experimental investigation indicates this. Is this a specific property or is it merely a special aspect of the general resistance of living organisms to foreign substances? There are certain well known processes by which an animal reacts to such stimuli. An inert sterile foreign body may be encysted by fibrous tissue. An irritating foreign body, such as a chemically active substance, or living cells of the bacterial or protozoan order, may induce and be resisted by a suppurative response. Certain other chemical substances may be combated by a specific chemical response in the nature of an allergic or immunity reaction. It has not been proved that the reaction to living mammalian cells fits exactly into any of these pictures. Certain inferences, however, may be made from the known facts. The increasing complexity of structure, function, and chemical internal environment met in the ascending animal series is parallel to the increasing difficulty of cross-grafting. This increasing complexity is, no doubt, associated with more and more exact specialization and individualization of the body cells to fit them to a highly specialized environment, and a corresponding further removal from the totipotency ascribed to such cells as the ameba and the early fertilized ovum. These changes affect cross-grafting in two ways. The cells grafted from another mammal have been highly adapted to their own original environment, and hence are less well equipped to adjust themselves to changes, even of comparatively slight degree. On the other hand, the internal environment of the host animal is a highly complex affair that is provided with a mechanism to maintain itself constant, which apparently includes defenses against even slightly alien chemical substances, such as might be brought in by the grafting of foreign mammalian cells. When one recalls the size, complexity, and variety of protein molecules, for example, it is quite conceivable that certain proteins in the living mammal and in its cells may exhibit slight modifications that are specific for that one individual, and that would excite intolerance and reaction in other individuals, even of the same species. There are some observations that suggest such a possible explanation of the resistance to cross-grafting. When human skin is grafted to another person, it often seems to do well for a number of days, and then usually rapidly dissolves and disappears. This strongly suggests a defense mechanism that requires an appreciable time to develop, and that is a direct response to the stimulus of the foreign tissue. In short, it looks like the development of something like a specific immunity reaction. Such an explanation fits better than simpler reasons that might be given, such as lack of nourishment to the graft, inflammatory reaction caused by it, or incidental complications like bacterial infection. If the defense mechanism proves to be in the nature of an acquired immunologic reaction, there are many further questions that arise. Is such a reaction mediated through the circulating body fluids or is it a property of the host cells, or do both cells and fluids take part in it? Is it a local or a general response? Is it specific against the type of grafted tissue alone, or is it equally effective against all tissues of the donor animal? Is it limited to cells from the original donor, or has there been set up a reaction that will now function

promptly against the same type of cells from any donor? Most important of all, if such a defense mechanism explains the intolerance of the mammal for foreign living cells, is there any way in which the defense may be broken down or set aside? There is also a possibility that nerve relations may play some part in the question of survival of cross-grafts. Indirect evidence of this may perhaps be read into the experiments of Schotte and Butler.⁶ These experiments indicated that when a limb of certain amphibian larvae is kept denervated, the capacity for regeneration after injury is lost. Not only does the amputated extremity of such a limb fail to grow out anew, as it normally would, but regression and resorption start from the level of the amputation and proceed proximally, often bringing about complete disappearance of the limb. There is so much superficial resemblance in this process to what often happens to foreign tissue grafts in adult mammals that it stimulates suspicion that the lack of nerve supply to the implant might play a part in its failure.

Our work includes experimental studies on laboratory and clinical material. It is being carried on by a group of my associates on the Surgical Service of the Johns Hopkins Medical School—Dr. James C. Owings, George O. Gey, Kenneth Pickrell, and Douglas H. Stone, and enjoys the hearty support of Dr. Alfred Blalock, head of the department. As sufficient material is developed, detailed scientific reports will be published. The purpose of this paper is to establish the problem and to lay down certain generalizations based on our own previous work and that of many others. The first point of emphasis is the effort to understand why implants of alien cells die, rather than the development of a specific successful grafting technic, which may be hoped for as a later result. Certain conditions essential for the success of implants do concern the details of technique, however, and may be summarized as follows, from one of our earlier publications.⁷ (1) Implants must be small, a few millimeters in diameter, otherwise the central portion dies before it can be vascularized. (2) The technique must be surgically sterile. (3) The bed to receive it must be near a good blood supply, but must not be too richly vascular, otherwise hematoma formation will choke the graft. (4) The bed should be of loose structure, otherwise tissue pressure will compress the graft. These points may be considered as established. Much more doubtful are two conditions that certain workers have thought to be necessary. (5) A physiologic need on the part of the host for the tissue grafted. (6) Anatomic correspondence of the bed with the site from which the graft is taken, such as thyroid grafts into the thyroid region of the host. So much for present knowledge of technical conditions.

The large experience of many zoologists permits certain conclusions of a general biologic nature. (1) Resistance to alien living cells is lowest in the lower forms of animal life and increases as one moves upward in the phylogenetic scale, this resistance being greatest in the mammalian group. (2) Resistance in any single species is lowest in the youngest forms and increases from embryo to old age. (3) Grafts are more apt to succeed the younger the donor individual, the best source being embryonic tissue. (4) The wider

the biologic diversity of host and donor the less likely is success of grafting, the best opportunity being between identical twins

In addition to the technical and general biologic conditions that affect the problem, there is finally the specific reaction of the recipient as related to the alien cells. At least two views have been advanced concerning the reaction of the host to the graft. One of these, on which much stress is laid by Loeb,⁴ emphasizes the more or less specific local tissue response about the graft, and the other regards the host reaction as essentially specific chemical in nature, similar to anaphylaxis or immunity. This brings us to the very kernel of the problem, and our work is far from that stage of advancement that would permit an answer as yet. However, enough has been accomplished to give us certain impressions. Thus, studies of autografts of thyroid in dogs show wide differences in grafted fragments made in the same way and at the same time. Some of these fragments are so well preserved as to look almost normal, and about them there is very little infiltration with leukocytes, lymphocytes, or other wandering cells. A short distance away, another fragment may show defective staining properties of the cells, breaking up of acini, and an accompanying active infiltration with leukocytes and particularly lymphocytes. Still another fragment may be completely hyalinized and imbedded in granulation and early scar tissue. To us it seems likely that the inflammatory reaction is not a defense against the grafts, *per se*, but merely the usual phagocytic response to damaged tissue. In other words, the cellular local reaction did not kill the grafts. Otherwise, all of them should be equally and simultaneously attacked. But some of the mechanical or technical factors, perhaps failure to establish blood supply in time, led to the death of certain fragments which are then removed by the well-recognized inflammatory local reactions. In short, we would interpret the local tissue reaction, not as a defense against living grafted cells, but as a scavenger reaction against dead cells.

There are a number of observations that have a bearing on the possibility that defense against alien grafts is in the nature of a chemical immunity in many cases. It was with this idea in mind that the writer, and his associates,⁷ some years ago, conducted a series of experiments. These consisted in growing for a considerable time fragments of the tissue to be grafted in tissue culture, on media containing the serum and plasma of the anticipated host. In this way it was hoped to adapt the grafts to their future chemical environment. Following these experiments on dogs, a number of human cross-grafts were performed in a similar manner, with apparently some definite success.⁸ Others have undertaken similar experiments with conflicting results—some successful, many not.⁹

It now appears to us, however, that a much better method is possible, and we are in process of developing it. As has been said, there have been many observations, both clinical and experimental, that alien grafts often seem healthy for a considerable time, perhaps two to three weeks, and then suddenly disintegrate. Such a phenomenon does not fit into our ideas either of an inflammatory reaction defense or of an immediately hostile chemical environment. In either, such form of resistance to the graft one would expect

a prompt and continuous destructive effect. It does suggest that the graft is the source of alien chemical substances, probably proteins that differ, perhaps not greatly, from those of the host, but sufficiently to act as antigens. In response to this stimulus, a defense mechanism is set in motion that produces antibodies, not originally present, that in time lead to the destruction of the alien cells of the graft. There are a number of experiments that suggest themselves as methods of testing the truth of this theory, and that we expect to carry out. There is also an obvious extension of our idea of adaptation of the graft to its environment that we also are planning to test. It consists in grafting a host with a given tissue and awaiting the development of the specific defense mechanism. Then we shall attempt to adapt the same tissue to the now stimulated host, in other words, to immunize the graft against the immunized host. We regret that much of this work is still only in the stage of development and that specific detailed reports must be deferred till some future time. Whether any of these experiments prove fruitful or not in leading to concrete results, the purpose of this paper will be attained if an aroused interest in the general problem develops.

Let us take a little time to consider the importance of this field and the opportunity it offers at the present. It would be an error to assume that other fields of surgical development have been exhausted, an error similar to that attributed to Pare, Billroth, Moynihan and Halsted, each of whom is said to have lamented the future of the young surgeons succeeding him, because all the great advances had already been made. Nevertheless, it is true that many fields of surgery are already extensively developed. In ablative surgery, the operative removal of offending lesions or organs, the greatest attainments have been achieved. Now that the skull and the chest are successfully invaded, not as a rare adventure, but as a routine, every-day performance, further progress would seem to be largely a matter of detail. No doubt better technique, better instruments, better preparation before operation, and better after-care will greatly improve results, but there are no remaining great anatomic areas for the expansion of ablative surgery. Reconstructive surgery in its various subdivisions—plastic, orthopedic, prosthetic—is still far from the stage of advancement that ablative surgery has reached. Here there are constant announcements of new achievements, and without doubt there still remains much opportunity for original development. But for those seeking a new frontier, a wide virgin country for exploitation, I would enlist your interest, your thinking, and your hard work in what may be called replacement surgery. As on every frontier, the going may be hard. As in every virgin territory, the clearing of the terrain may be backbreaking and heartbreaking, with delays, disappointments, hope deferred. It will call for toil and sweat, if not for blood and tears. But the promised reward is great. To take a single example, consider the possibilities, if we can overcome resistance to alien mammalian cells, in the whole group of endocrine deficiency diseases—a definite cure for parathyroid tetany for myxedema, for Addison's disease, perhaps for diabetes, and possibly for other conditions not now understood. The replacement of entire

organs, useful and functioning, is not impossible. The vascular and ureteral hook-up of a new kidney could be accomplished, if the kidney would live after it had been implanted. These are obvious potential results of a conquest of the resistance of the human body to alien cells, and if the imagination be allowed free rein, they are but the beginning. There is no need, however, to exaggerate the results that might follow such a success. My purpose is accomplished if you give this plea the importance I think it deserves.

We hear much these days of military matters. There is a certain analogy between the methods of scientific attack and military offensive. The army feels out its opponent, finds weak spots, drives in a wedge here and a column there, develops a pincer movement, surrounds an area, and then reduces it. So in science, a lead in one field, an original idea in another, a new technique, a better instrument result in advances that stimulate each other. But in war, field tactics are not enough. One may win battles and lose the war unless there is a broad view, a general strategy. In science also, it behooves us to think at times beyond the day's work and the immediate problem, to survey the whole front and its hinterland. In such a survey, local issues will fall into their proper proportions and the larger strategic problems will emerge. One of the functions of such a body as the American Surgical Association is to act as a general board of strategy in its own field. The object of this paper is not to record a local advance, but to bring up for consideration a major problem—that of the reaction of the human body to its own and other mammalian living cells. Perhaps such a purpose today may seem visionary, but let us not forget that often in the story of mankind the visionary of to-day has proved in some distant tomorrow to have been the man of vision.

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REPORT TO THE AMERICAN SURGICAL ASSOCIATION
ON
ACTIVITIES OF THE DIVISION OF PROFESSIONAL SERVICE

UNDER THE SUPERVISION OF
THE SURGEON-GENERAL OF THE U S ARMY

BY
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WHEN OUR PRESIDENT, Doctor Stone, invited me to make some remarks on the activities of the Division of Professional Service, under the Surgeon-General of the U S Army, it seemed wise to commit my thoughts to writing in the interest of both brevity and accuracy

As you know, the function of the Surgeon-General's Office is to provide adequate medical service for the Army at posts, camps and stations within and, on occasion, beyond the continental limits of the United States

This makes for a very diversified type of medical service, extending from tactical units in the field to the general hospitals far in the rear That all types of medical men are essential to the proper functioning of the Corps, is admittedly obvious, and the diversification of duties requires not only trained general practitioners and men just out of their intern-year but also specialists in every field of medicine and surgery The Division of Professional Services of the Army has many activities, and the one which is of the most interest to you is the Subdivision of Surgery

The duties of the Subdivision of Surgery may be outlined briefly as follows (1) Coordination and supervision of professional care (surgical), which includes inquiries, complaints and investigation (2) Advisory duties concerning equipment, training and personnel

With the huge expansion of the armed forces, a concomitant multiplication of medical officers becomes inevitable, and if many of the problems which face the profession seem to be handled with some tardiness and delay, it should be remembered that confusion is inevitable under circumstances of an emergency in a democracy When the training program for the present military forces was inaugurated, the Regular Army Medical Corps numbered approximately 1,210 officers There were in addition about 1,150 National Guard Medical Officers and a Medical Reserve Corps of some 16,000 to 17,000 men who were immediately available to staff medical installations of the Army, and these were mobilized in a short time There are now on duty between 12,000 and 13,000 medical officers and, with the increase of the Army as authorized at present, it is estimated that 24,000 medical officers will be essential to render proper service to the armed forces by the end of 1942 In addition to this, the Surgeon-General has recently made an appeal for 6,000 medical officers to supply the medical needs of the developing air force To this

should be added the recent recommendation of the Surgeon-General for the commissioning of an additional 7,000 medical officers for our immediate needs, three in the grade of Colonel, three in the grade of Lieutenant Colonel, 300 in the grade of Major, 1,000 in the grade of Captain, and 5,647 in the grade of First Lieutenant. I stress the grades in which these men are to be commissioned to emphasize that this is a young man's war, that it is enormously more strenuous and exacting of stamina than World War I, and that for the immediate future it is necessary to commission a large number of younger officers for service with tactical units. These men will be drawn from interns who complete their service in July of this year, and from the men who are under 36 years of age and subject to the action of selective service.

While it is necessary to emphasize again that this is a young man's war, it should be pointed out that a large percentage of the volunteers for medical service, up to the present time, have been in the older-age groups, many of whom served in some capacity in the last war and who are young enough and able economically to give up practice and take active service now. Probably this is not the wisest thing under the circumstances, and it should be emphasized that the older generation's function is primarily one of taking care of the civilian population, of manning the medical schools of the country and, therefore, insuring the maximum output of medical men without a lowering of standards. It would not be amiss for these older men to bring to the attention of the younger physicians that they are needed by the armed forces rather than the older group, and that theirs is a distinct obligation to serve their country for these two reasons.

However, there are other points which I wish to make in discussing allocation of specialists in war surgery, which will be familiar to those of you who served in the last World War.

(1) You will recall that war surgery differs materially from civilian surgery, that it is not elective surgery but surgery of catastrophe.

(2) That there is no continuous flow of cases, but periods of long arduous duty followed by periods of complete absence of professional work.

(3) That the Army requires many professional duties completely foreign to a specialist whose specialty may be narrow in its scope.

If these facts can be remembered and buttressed by the knowledge that one has to do a patriotic service, albeit a distasteful one, I believe that civilian medical men will meet on a more common ground with the Regular Army personnel and find fewer reasons for irritation and criticism. Actually, surgery of all kinds will be done, and it will have to be done by younger men under unfavorable conditions, but out of this war, as out of others, will emerge some surgical principles which will be advantageous to future civil practice.

Another fact which emphasizes how much of this present action is a young man's war, is the type of warfare which is being waged. In a recent conversation with Colonel Gillespie, of the British Army, who has served in the Middle East and in Libya and, indeed, from all of the literature by such men as Jolly and Trueta, I have been greatly impressed with the necessity

of transporting the surgeon to the patient in the vast majority of cases rather than the reverse, which has been the practice in the past. The war of movement, where the favorite tactics revolve around widespread encircling types of maneuver, results in fewer casualties, perhaps, in killed and wounded, but in an enormous increase in the number of prisoners and missing. Because of the vast distances involved, it has been found necessary to insist on the greatest mobility of hospital installations in the theaters of operation, which means the increased use, therefore, of operating teams in small units, which are quickly and readily transportable. This streamlining throughout the entire pattern of modernized warfare has changed many hitherto set practices in the care of the sick and wounded in the advanced areas. Thus, with the lessons of the Allies in front of us, unquestionably, we should be quick to modify many of our now accepted beliefs in matters of medical organization.

Another point of enormous interest to you is, I am sure, the proper utilization and allocation of specialists. The Surgeon-General's Office has definitely recognized the sphere of usefulness of highly trained men in different specialty branches, and has adopted a policy of commissioning these men in grades commensurate with their age, training, and professional capacity.

As you know, it has been customary in the past to make all first appointments in the Medical Corps in the grade of First Lieutenant, save only for definite exceptions which relate to professional training, and I quote "Captains, eligible applicants" (1) Eligible applicants between the ages of 37 and 45 will be appointed to the grade of Captain by reason of their age and general medical training and experience. Exception. Below the age of 37 the following training and experience will be considered in recommending initial appointments in the grade of Captain: (1) Certification by an American Specialty Board, (2) fellowship in the American Colleges of Surgery or Medicine, (3) membership in other recognized specialty societies or associations, (4) training equivalent to that required for examination by an American Specialty Board, and (5) other recognized training appropriate to the position for which recommended.

For the grade of Major eligible applicants are usually between the ages of 37 and 45, where vacancies exist, but men may be qualified for commission to this grade who have had the additional training and experience mentioned above.

There are obviously but few assignments in the grades of Lieutenant Colonel and Colonel, since a considerable number of men in these grades, on a Reserve Corps status, have not yet been called to duty because positions available for them commensurate with their rank are not at the present time open. This policy, I think, definitely indicates the great desire of the Surgeon-General's Office to obtain and utilize the best professional talent in a manner which will insure maximum professional efficiency to the sick and wounded of the armed forces.

Distribution of personnel and allocation of specialists are complex problems which will not, and cannot, be immediately solved to the entire satisfac-

tion of either the specialists or the Army, but I think tolerance, patience, and understanding of the difficulties of an enormous and hurried expansion should be the attitude of both the profession and the Army toward these changes of status

In the 14 general hospitals now operated by the Medical Corps of the Army, the organization of the services is on a high plane, and the availability of additional specially trained medical men will unquestionably improve as time goes on. The general hospitals which I have visited in my short service in the Army during this war have been staffed in an extraordinarily efficient manner. I do not mean to say that they function in all specialty departments with the smoothness of a civilian hospital of long standing or those associated either with a medical school or group practice, but I have found splendidly trained men in charge of the services, and that professional work of a high character is being rendered.

In the station hospitals and smaller installations, a larger number of professional men are being utilized, and constant effort is being made to readjust professional services in order that the selectees, as well as the officer personnel of these particular posts and cantonments, may have available to them medical care comparable to that of the best civilian practice.

In short, one of the aims of the Division of Professional Service is to fit men who are properly trained into key positions and avoid, insofar as possible, the often repeated, and sometimes justifiable, criticism of putting round pegs into square holes. I can testify, unreservedly, to the wholehearted cooperation which is evidenced in the Office of the Surgeon-General, and I can assure you that there is every indication of a real desire to utilize professional men in professional capacities to a maximum extent, and of avoiding, insofar as possible, pitfalls which developed in a similar rapid expansion during World War I. It is my considered opinion that many lessons of that mobilization and subsequent periods of operation have been learned and are being applied zealously in an effort to smooth out many of World War I's unpleasant irritations and inequalities.

I am confident that medical care throughout the period of mobilization, training and active participation in the present conflict will be far superior to that rendered in the past, and that this will be the result of the hearty support of the medical profession as a whole, and such associations as this in particular.

A striking example of modern medical efficiency in war is at hand, as demonstrated in the Pearl Harbor engagement, an account of which most of you have had from Doctor Ravdin and Doctor Perrin Long. Suffice it to say that here was an ideal set-up where in the first place the terrain was favorable, where the men were not in many instances clothed with heavy, dirty clothing, puttees and shoes, and where medical attention was immediately available within a few minutes of attack. In addition, the hospital facilities were accessible, transportation was ready and surgery was instituted in periods of from a half-hour up to many hours. The Chief Surgeon had anticipated the medical

requirements of an attack on the islands and had organized both in the military and civilian profession operating teams which became immediately available for service. The factors of immediate aid, rapid transportation, thorough debridement, plus the use of chemotherapy, and the treatment of shock by use of blood plasma and other mechanical means, are reflected in the brilliant results obtained following this battle. Subsequent inspection of the casualties has borne out the belief expressed by the early observers that, given adequate early care, proper treatment of shock, complete debridement, and the lavish use of sulfonamide drugs, we may expect a distinct lowering of mortality statistics, with a concomitant increase in the ultimate number restored to duty, or at least, saved from permanent disability.

Again, I should like to tell you that it would be difficult to overestimate the influence and helpfulness of many professional organizations in this present period. Surgical committees and various subcommittees of surgical and medical specialties, under the Medical Division of the National Research Council, have contributed efforts and advice which have been of inestimable advantage, and I can assure you that I have seen every inclination on the part of the Surgeon-General's Office to utilize these efforts to the fullest, and to accept professional advice when offered by such groups at its face value.

Today, there is no question that we are much further forward in this war, insofar as medical personnel and services are concerned, than we were in the middle of World War I. I have no illusions that professional services will be conducted to the complete satisfaction of everyone concerned, for the very individualism of our profession militates against that, and when such individualism collides with Army regulations it is certain that compromise is the only method whereby efficiency can be maintained.

In consequence, I would urge upon medical men everywhere the fact that tolerance and patience be a part of their credo, which must recognize certain inevitable dislocations of life and methods in such times of emergency.

It is our duty and desire to render to every American soldier adequate medical care. He deserves it and he should have it. I know that this is your promise as it is mine.

SYMPOSIUM ON ABDOMINAL SURGERY

TRANSTHORACIC RESECTION OF TUMORS OF THE STOMACH AND ESOPHAGUS*

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THE particular region of the alimentary tract with which we are concerned is that which begins in the esophagus at the junction of the base of the neck with the superior mediastinum and extends to a point several centimeters below the cardiac orifice of the stomach. An arbitrary division of this segment of the alimentary canal into three zones can be made as shown in the diagram (Fig. 1). The classical division of the esophagus has always been into thirds. It is our observation that both from the standpoint of the site of occurrence, and from the point of view of surgical management, it is more useful to divide it into fourths. The second and third fourths are to be thought of as the middle half.

Zone 1 extends from the base of the neck to the superior surface of the aortic arch. Removal of a growth situated in this portion of the esophagus (an uncommon location, fortunately) is a specialized problem, the management of which is not yet clear. The proximal esophageal end is so short that the establishment of an external fistula may be impracticable. The highest practical level for division of the esophagus with the construction of a suitable cervical esophagostomy is just above the superior surface of the aortic arch. If cut there, the proximal end when brought out in the neck will lie 1 or 2 cm. above the level of the clavicle. At this point the epiglottis can easily be felt by digital palpation down the lumen, and because the epiglottis is so near, a rubber tube can be worn only with great difficulty or not at all. Furthermore, a stoma located above the clavicle adds greatly to the technical difficulty of constructing an external esophagus by skin plastic procedures.

Zone 2 may be said to embrace the middle one-half of the thoracic esophagus, that portion extending from just above the aortic arch to a point just below the level of the inferior pulmonary veins. Growths in this region make it necessary to divide the esophagus at too high a level to allow the performance of an esophagogastric anastomosis. The only operation for carcinoma in this region is a partial esophagectomy which makes it necessary to bring the proximal end of the esophagus to the surface in the upper part of the chest by pulling it out through a cervical incision. Feeding is carried out by artificial means through the exteriorized lower end of the esophagus or through a gastrostomy, or eventually by swallowing through a rubber tube connection between these, or finally through a skin-plastic tube constructed to bridge the gap between the stomata.

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942.

Zone 3 includes the lower one-quarter of the thoracic esophagus, the cardiac orifice of the stomach, and the adjacent few centimeters of the stomach including the fundus. Lesions located in this area are low enough to make it possible to perform an anastomosis between the esophagus and a portion of the stomach. Certain high gastric carcinomata involving a portion of the esophagus, which if approached through an abdominal incision will be inoperable, can be successfully removed through the transthoracic route. Resection with esophagogastric anastomosis is an extremely useful operation in certain cases for both esophageal and gastric carcinomata.

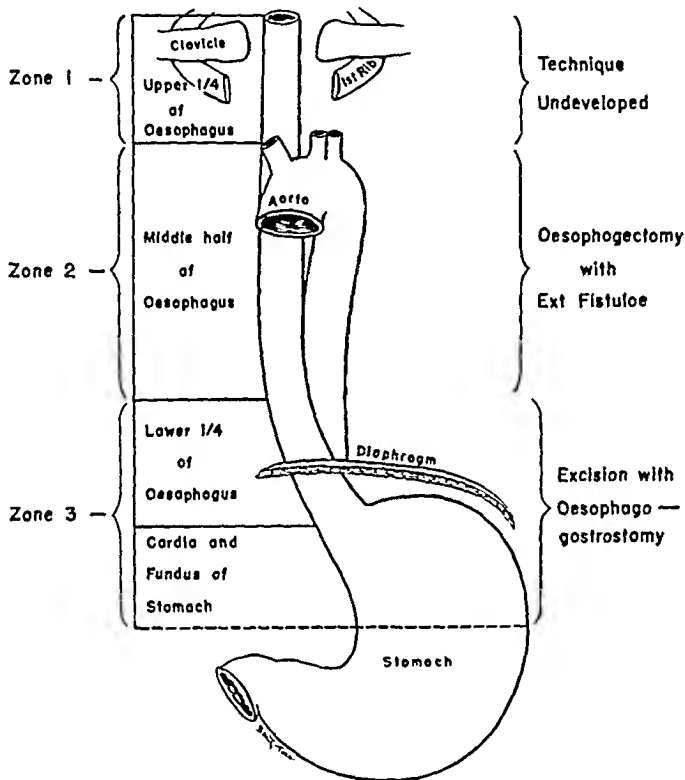


FIG. 1.—The arbitrary division of the thoracic portion of the esophagus and the cardiac region of the stomach into zones so as to facilitate the understanding of the technical problems involved in the surgical management of carcinoma arising in these several areas.

Pathologic Considerations

(1) The majority of carcinomata of the esophagus are epidermoid in character. The change from squamous to columnar epithelium usually becomes obvious at the cardia, but in certain cases mucosa of the gastric type may be found in the lower esophagus. This appears to explain the rare case of an adenocarcinoma confined entirely to the esophagus. Case 7 of this series is an example.

(2) Carcinoma arising in the esophagus often spreads in the submucous and muscular coats of the organ for a distance of several centimeters in such a way that it can be detected only by microscopic examination. This was observed in several of the cases. A noteworthy example is that in Case 3

where at a plastic operation done in preparation for the making of an external esophagus, definite microscopic extension of the tumor in the lower esophageal stoma was found in a section removed for examination

(3) A third fact concerning the pathologic behavior of carcinoma of the esophagus is the great frequency of metastases to the lymph nodes below the diaphragm. The lymphatic drainage from the esophagus, though not thoroughly understood, may be assumed to follow in a general way the course of the vascular supply. In the upper portion the blood supply is from the inferior thyroid artery. Here the cervical nodes tend to become involved. From the level of the aortic arch down there is an increasing tendency for metastases to occur to the nodes in the region of the left gastric vessels. An analysis of the cases of carcinoma of the thoracic esophagus which came to autopsy in the 43-year period 1897 through 1940, reveals the fact that of 24 cases of carcinoma in the upper third only one showed metastases to nodes below the diaphragm. In 32 cases where the growth involved the middle third, 11 showed metastases to the subdiaphragmatic nodes. Finally, of 16 lower third growths, eight showed positive nodes below the diaphragm (Table I).

TABLE I
METASTASES TO SUBDIAPHRAGMATIC LYMPH NODES IN 72 PATIENTS WITH CARCINOMA
OF THE THORACIC ESOPHAGUS*

	No. of Cases	No. with Metastases
Carcinoma of upper third	24	1
Carcinoma of middle third	32	11
Carcinoma of lower third	16	8

* From the autopsy records at the Massachusetts General Hospital 1897 through 1940

A knowledge of this fact is, of course, of great importance in deciding about the probable curability of these cases. It may well be considered unjustifiable to subject a patient who already has metastases to these distant nodes to the mutilating procedure of esophagectomy when the likelihood of cure must be so slight. On the other hand, the striking palliative results of resection with establishment of an esophagogastric anastomosis gives a wide latitude to this operation even in the presence of distant metastases.

(4) Metastases to the liver in cases of carcinoma of the esophagus occur very late in the disease.

(5) Metastases to the lung should always be looked for because the venous return from the high gastric and esophageal areas enters the caval system directly instead of passing first through the portal system.

Determination of Operability

Exclusive of the usual considerations relative to the age and general condition of the patient, certain observations and diagnostic procedures are important.

(1) *Clinical Observations* (a) A constant boring pain in the interscapular region of the back is often an indication that carcinoma of the esophagus has reached an inoperable stage.

(b) Persistent fever is usually an indication of inoperability in carcinoma of the esophagus or cardiac end of the stomach. It occurs as a result of infection in a deeply eroding or ulcerated growth.

(c) Rectal examination when the growth is primarily in the stomach may reveal a rectal shelf of peritoneal implants.

(d) Supraclavicular lymph node involvement is less common than was anticipated.

(2) *Endoscopic Findings* (a) Esophagoscopy is essential to determine the nature and level of the lesion and especially to procure tissue for microscopic diagnosis. But endoscopy cannot give information concerning the degree of extension of the growth in the layers below the mucous membrane.

(b) Gastroscopy has been of limited value in lesions of the fundus of the stomach as it is difficult to see the primary growth. In five cases of carcinoma of the cardia or fundus, the growth was visualized through the gastroscope in only two cases. In the remaining three cases it was not seen.

(c) peritoneoscopy as an aid in the determination of operability proved of no value in the six cases in which it was performed. In an occasional case of widespread abdominal metastases or liver involvement, a peritoneoscopy may save the patient a major exploration. When widespread metastases have not occurred, peritoneoscopy is of no value because it is impossible to see the retroperitoneal nodes in the region of the left gastric vessels or even the lesion itself.

(3) *Roentgenologic Examination* Roentgenologic visualization by a radiologist especially interested and skilled in the technic of examining the esophagus has been found to be of the greatest value in localizing the lesion and in predicting the degree of extension of the growth. Everything considered, the roentgenologic examination has been of more value than any other diagnostic procedure.

Preoperative Preparation of the Patient

Adequate time is taken to bring the patient's general condition to its optimal point. Oral sepsis is eradicated if possible before any serious gastric or esophageal operation is undertaken. A high vitamin, high protein, high carbohydrate diet is administered. Transfusions sufficient in number to restore the blood to a relatively normal level are important. Preoperative artificial pneumothorax is not necessary or advisable.

An intravenous infusion of glucose and saline is started immediately before the operation is begun.

MANAGEMENT OF CARCINOMA OF THE MIDDLE PORTION OF THE THORACIC ESOPHAGUS (ZONE 2)

A malignant lesion in this portion of the esophagus makes it necessary to resect at so high a level that an esophagogastric anastomosis is impossible even if the stomach is mobilized by cutting the vasa brevia, the left gastroepiploic, and the left gastric arteries. The highest anastomosis in this series was done at the level of the aortic arch. Elevation of the stomach to this

height was facilitated by a preexisting hiatus hernia. Usually it is impossible to carry out an anastomosis without a dangerous degree of tension if the stomach is elevated above the level of the inferior pulmonary vein. Anyone who has had the experience of dividing the esophagus is familiar with the extraordinary degree of retraction which takes place.

When the thoracic esophagus is to be completely resected and a cervical esophagostomy established, it is necessary to provide an enterostomy for feeding. There are several advantages which accrue from considering enterostomy as the first step in the surgical program. The enterostomy may be (a) temporary in the form of a jejunostomy if it is planned ultimately to bring the lower end of the esophagus down from the mediastinum and use it as the gastric stoma, or (b) permanent in the form of a gastrostomy which is suitable for use in plastic reconstructive procedures.

The procedure for surgical removal of a carcinoma in the mid-esophagus must be divided into two or more stages which may be grouped as follows:

First Phase of the Operation

A muscle-splitting incision is made in the upper portion of the left rectus muscle. The liver is palpated. A careful investigation of the lymph nodes in the region of the left gastric vessels is then carried out. Enlarged nodes are removed for frozen section biopsy. Of 23 cases of carcinoma of the thoracic esophagus explored in this manner since January 1940, 12 have been found to have metastases in these nodes. A palliative gastrostomy may then be carried out and the surgical program closed. If there are no liver or lymph node metastases which cannot be removed with reasonable hope of arrest of the disease, the first stage is completed by the establishment of a jejunostomy or gastrostomy, depending upon the plan for completion of the operative procedure.

A jejunostomy is performed if it is planned to use the short segment of the esophagus just above the cardia for the permanent lower stoma. This requires a second celiotomy following the esophagectomy. A lower stoma made from the stump of the esophagus has certain merits, but also serious drawbacks. There is a rapid and kind union of the stratified esophageal mucous membrane with the skin of the abdominal wall which minimizes troublesome fistula formation during the construction of a skin-tube esophagus. On the other hand, the stoma tends to be small and a delay in the passage of food from the skin-tube to the stomach has been observed at this point in one case (Case 1). We have abandoned the use of the esophagus for the lower stoma, however, for a more serious reason. The extension of cancer in the submucosal lymphatics to some distance from the palpable or visible growth has been pointed out. Preservation of any portion of the lower esophagus for reconstructive procedures may lead to the disaster of inadequate cancer surgery. A recurrence in the stoma is recorded in one patient (Case 3).

We now recommend a Beck-Jianu gastrostomy at the time of the ab-

dominal exploration. The lower stoma of the gastric tube can be brought several inches above the costal margin on the anterior thoracic wall. By taking care to construct the tube with a large diameter this type of stoma is ideal to receive the lower end of a rubber connecting tube. It is satisfactory also for the construction of an external esophagus from the skin. Experiences with this aspect of the problem are exemplified in Cases 5 and 7. The technic of the Beck-Jianu gastrostomy has been described elsewhere¹ (Fig 2)



FIG 2—The stomata after esophagectomy for carcinoma of the midportion of the thoracic esophagus. Upper stoma is esophagus. Lower stoma is the end of a Beck-Jianu gastrostomy.

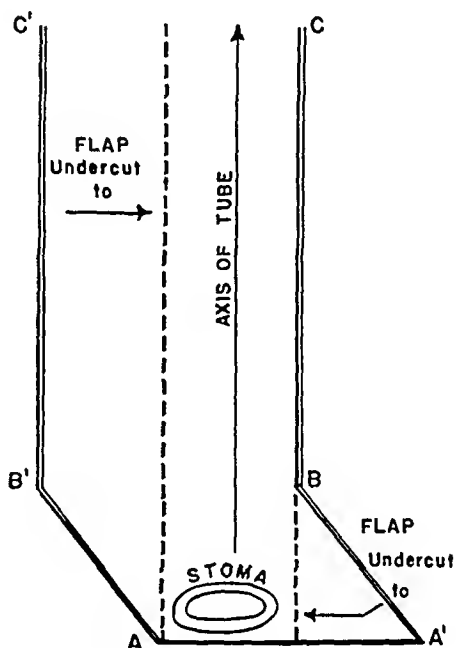


FIG 3—A convenient method for constructing skin-lined tube esophagus around stoma. Suture A to A, B' to B and C to C. Tube can be stopped with open end at any point without leaving denuded area. This can best be visualized by cutting pattern is outlined above and folding on dotted lines.

Second Phase of the Operation

After the patient has recovered well from the preliminary abdominal operation, the growth is removed by a transpleural esophagectomy. Whether the approach should be right-sided or left-sided is debatable. That a growth located opposite the aortic arch can be reached more easily from the right side must be granted. But when working through the left side the aortic arch can be retracted sufficiently well to obtain direct access to a growth in this area by dividing the upper intercostal arteries. This is mentioned by Torek in his original article². If the right side is used, it is necessary to do a preliminary mobilization of the esophagus in the neck as a separate stage before attempting the esophagectomy. If the left-side approach is used, the cervical portion of the operation can be done at the time of the resection, thus avoiding a separate procedure. Better access to the upper end can be had

from the left side. The determining consideration that leads us to recommend that esophagectomy be done through the left pleural cavity is the greater ease of access to the lower three inches of the esophagus. The fact that cancer infiltrates the muscular wall of the esophagus for a considerable distance away from the obvious growth makes it imperative to divide the organ as far away from the tumor as possible. Added to this, the frequency of lymph node metastases below the diaphragm as mentioned above (12 out of 23 cases) makes it advisable to open the diaphragm, divide the stomach just distal to the cardia, and excise the lymph nodes in the region of the left gastric vessels. By this procedure the entire organ with the majority of its regional lymph nodes is resected—an established principle of cancer surgery.

A description of the technic of this stage of the operation is as follows:

Technic of Operation

With the patient lying on his right side, a long oblique incision is made across the left side of the chest over the course of the seventh or eighth rib, resecting the rib from the costal cartilage to its articulation with the transverse process of the vertebra. Adjacent ribs may be divided near their necks by excision of short segments to afford the desired exposure. The pleura is incised and the anesthetist reduces the endotracheal pressure to allow the lung to collapse. If the lung is adherent it is freed enough to be retracted medially. Large gauze pads are used to protect the wound edges and a rib spreader is inserted.

With the lung retracted medially the mediastinal pleura over the esophagus is incised from the diaphragm to the aortic arch. By blunt dissection the esophagus is mobilized and a tape passed around it for retraction. As the esophagus is further mobilized the esophageal branches of the aorta are ligated and divided. One or two small branches from the left bronchial vessels must be divided. The esophagus is cut across as low as possible and the distal end is inverted with silk sutures. In the complete operation the esophageal hiatus of the diaphragm is enlarged by dividing muscle fibers and the cardia delivered into the thorax. The esophagus is divided at the cardia and the defect in the stomach wall closed. After removal of the esophagogastric cluster of lymph nodes the diaphragm is sutured. A finger cot or small sheet of rubber is tied over the cut end of the esophagus.

The mediastinal pleura above the aortic arch is incised at a point posterior to the left subclavian artery. The esophagus is mobilized by dissection at this point and another tape passed around it. By working now from above, now from below the aortic arch, that portion of the esophagus which lies behind it is liberated. If necessary, better access to this portion may be obtained by dividing one or two of the upper intercostal arteries to allow retraction of the aortic arch forward and to the left, away from the esophagus. In order to free the esophagus completely, the vagus nerves are separated from it, but if one or both are inseparably adherent to the growth, they are divided. The esophagus is then pulled up from behind the aortic arch.

The next step is to make a small incision in the lower portion of the neck

along the anterior border of the sternomastoid muscle. The dissection is carried down to the prevertebral fascia, retracting the carotid sheath laterally. It may be necessary to ligate and divide the lateral thyroid vein. The attachments of the esophagus in the base of the neck are freed by dissection with the finger from above and below, creating a passageway from the thorax to the neck. A rapid alternative way to complete this step is to mobilize the esophagus in the lower portion of the neck by blunt dissection with the finger from within the thorax. A short cervical skin incision made by an assistant then gives ready access to the passageway thus created from below. A tape on the end of the esophagus is passed up from the chest and out the cervical incision and the esophagus is delivered in its entirety. If a bulky friable growth is present, it may be desirable to divide the esophagus above it rather than attempt to force the entire organ through the cervical tunnel. The upper end is then delivered into the neck and the lower esophagus, including the growth, removed through the chest incision.

Interrupted silk sutures close the mediastinal pleura. A layer-by-layer closure of the chest incision is made by interrupted silk sutures, taking care that the lung is fully reexpanded before the chest is made air-tight. Sulfanilamide crystals may be spread over the pleural surfaces and mediastinum before closure. Drainage is not used.

After the dressing has been applied to the thoracic incision, the patient is turned on his back for the completion of the operation as follows. The growth-bearing portion of the esophagus is removed with ample margin, taking care to cut across the viable portion of the esophagus which at that level is determined by the blood supply of branches from the inferior thyroid arteries. Taking note of the remaining length of the proximal end, a short transverse incision is made through the skin of the upper thorax, below the clavicle if possible, and the end of the esophagus is drawn down through a subcutaneous tunnel and out through this incision. A few fine silk sutures are loosely applied to anchor it. The cervical incision is then closed. The positive pressure within the trachea must not be released before the neck incision is closed because there is a direct communication through the neck and superior mediastinum with the left hemithorax. At the end of the operation examination is made for residual pneumothorax on both sides. Large collections of air are removed by aspiration.

Care of the Patient after Esophagectomy—The patient is kept in an oxygen tent during the first 24 to 72 hours or until it is obvious that there is no embarrassment of respiration due to pneumothorax or the accumulation of fluid within the chest. A small effusion need not be removed, but aspiration may be necessary if it is large. After 24 hours, small feedings are started through the gastrostomy and regular gastrostomy feedings are resumed as rapidly as the condition of the patient will allow.

The upper esophageal stoma may be allowed to empty into a large dressing of gauze which is changed frequently. As an alternative, a rubber tube is fastened into the end of the esophagus. In one case the pressure of the inner end of the tube produced a small area of necrosis and a fistula through the

wall of the esophagus near the stoma resulted. A troublesome local cellulitis developed. After ten or 12 days a soft rubber tube may be used to connect the esophageal stoma above and the Beck-Jianu gastrostomy opening below. In low-lying growths the proximal end can be left long enough so that the stoma will reach below the clavicle. In such cases a rubber tube connection serves very well. On the other hand, if the growth is high (opposite the aortic arch or above, the proximal end will be so short that it will come only to the surface of the neck above the clavicle where it is exceedingly difficult to apply a rubber tube because of the proximity of the epiglottis, the motions of the neck, and the angle of the esophagus with the skin. Furthermore, a rigid, angulated tube of glass cannot be made to fit well or to stay in place easily.

Patients are surprisingly comfortable, considering the mutilation to which they have been subjected, and recovery is usually rapid. On the average they are able to be out of bed by the tenth or twelfth day after operation.

Subsequent Course—Following the esophagectomy, the patient may be allowed to return home wearing a rubber tube between the stomata. Through this, liquid food can be ingested, and in

one notable case (Case 3) the patient ate soft solids and ground meat, washing them down with draughts of fluid. As a rule patients gain weight and strength. But they are not a happy group as a whole. They often fret at their inability to eat a normal solid diet and complain of the annoyance of the daily care of the rubber tube. It would seem from the humane standpoint, therefore, that one should look forward in every case toward the completion of an external esophagus by some type of plastic procedure.

Third Phase of the Operation

Many methods have been proposed for the construction of an external esophagus from skin, stomach, colon, or jejunum. Usually the skin of the anterior thoracic wall can be used successfully, but the details of the problem vary from case to case. The construction of a skin tube is more easily accomplished in women than in men. In men the skin is tighter and less



FIG. 4.—Case 6. The completed external esophagus. The prominence opposite the lower portion is caused by the fundus of the stomach.

freely movable. Furthermore, in many cases there is too much hair to make it advisable to turn in the skin most readily available. In one such patient it was estimated by counting the number per square inch that there were 1,500 coarse hairs growing in the rectangular area of skin which would have been required for the tube between the stomata. In this case (Case 5), with the help of Dr. Bradford Cannon, a tube of skin with a pedicle at each end has been constructed from the right side of the chest in the midaxillary line where there is no hair. This tube is to be transplanted and eventually connected to the two stomata.



FIG 5—Case 6. The completed external esophagus filled with barium taken by mouth.

In two cases a functioning extra-thoracic esophagus has been completed by turning in a tube of skin (Cases 1 and 6). In the first of these (Case 1), the lower stump of esophagus was used as the stoma in the epigastric region. In the second case (Case 6), the upper half of the stomach with a short end of esophagus attached was brought up over the anterior chest wall through a subcutaneous channel. By this means the lower esophageal orifice was brought up to the level of the nipple and a shorter skin tube was required. The functional result in the latter case has been slightly better than in the former.

In a fourth case, using a Beck-Jianu gastrostomy stoma for the lower end, a skin tube esophagus was almost completed (one stage only lacking) when the patient died of pneumonia (Case 7).

The case histories may be consulted for certain details of these plastic procedures.

Summary of Experience with Surgical Treatment of Carcinoma of the Midportion of the Thoracic Esophagus (Zone 2)

From February, 1940 to February, 1942, 21 patients with carcinoma of the midthoracic esophagus have been considered possibly suitable for resection (Chart 1). In all of these a preliminary exploratory celiotomy was performed. Twelve of these patients were excluded as candidates for esophagectomy because of the presence of lymph node metastases below the diaphragm. Of the nine cases without positive nodes below the diaphragm, one died of pneumonia before the chest could be explored. Eight patients of this group of 21 came to thoracic exploration. Of these, two were found to have a locally inoperable growth and resection was abandoned. Resection was

carried out in six cases. Of these, one died postoperatively of a cerebral accident.

Of the five patients who survived the esophagectomy, one has since died of distant metastases, and one died of pneumonia during the process of making an extrathoracic esophagus. Of the three ultimate survivors, one is living and well with a completed external esophagus, another is so content with his

Fate of 21 Patients with Carcinoma of the Mid Portion
 of the Thoracic Esophagus Selected from a Larger
 Group as being Probably Favorable for Resection
 February 1940 to February, 1942

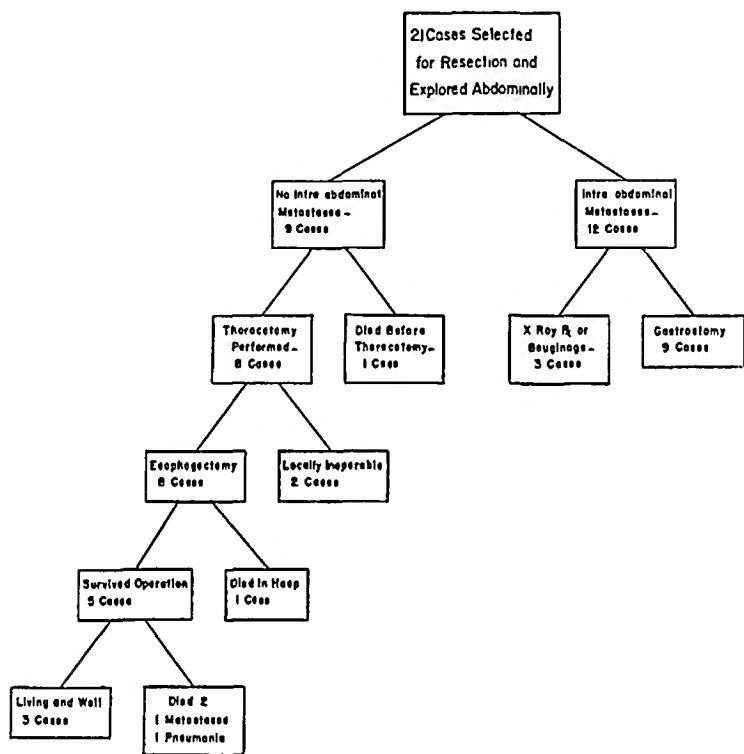


CHART I

rubber tube connection that he has thus far refused to consent to the making of a skin tube, and the third is in the process of having an antethoracic skin tube esophagus constructed.

TABLE II

CASES OF CARCINOMA OF THE MIDPORTION OF THE THORACIC ESOPHAGUS (ZONE 2)

Name	Date	Age	Operation	Result
E P	1938	43	Esophagectomy	Alive with metastases External esophagus completed
E C	1939	63	Esophagectomy	Died postoperatively
R B	1940	48	Esophagectomy	Died with recurrence
C W	1940	53	Esophagectomy	Died with recurrence
A M	1940	59	Esophagectomy	Well External esophagus partially completed
J L	1940	48	Esophagectomy	Well External esophagus completed
P L	1941	57	Esophagectomy	Died 4 mos after operation
J G	1941	72	Esophagectomy	Well
B L	1942	68	Esophagectomy	Died postoperatively

Table II shows the total group of nine cases of carcinoma of the mid-thoracic esophagus in which an esophagectomy was performed, including the three cases done before February, 1940. These three were not mentioned in

the above analysis because of lack of investigation of the abdominal lymph nodes at the preliminary abdominal operation

MANAGEMENT OF CARCINOMA OF THE LOWER ONE-FOURTH OF THE THORACIC ESOPHAGUS AND CARDIAC END OF THE STOMACH (ZONE 3)

A growth located in or near the cardiac orifice of the stomach, if operable at all, can be resected and an anastomosis made between the proximal end of the esophagus and the stomach. This operation utilizes a transthoracic approach through the diaphragm and is employed for certain low esophageal and high gastric carcinomata, in other words, for any growth in Zone 3 as defined above. A carcinoma of the cardiac orifice of the stomach usually involves grossly or microscopically, the lower end of the esophagus so that resection with a margin of safety is a technical impossibility if the conventional abdominal incision is employed. The technical advantages of the approach through the chest include greater ease of access to all of the structures involved in the procedure, the possibility of removing a longer segment of esophagus, and the avoidance of a total gastrectomy in the high gastric cancer group.

In comparison with the abdominal approach to this region, data collected by the Anesthesia Service indicate a more stable maintenance of vasomotor equilibrium even though the actual operation may be of longer duration. It is also our impression that postoperative pain and pulmonary complications are lessened. Certainly they are no greater.

Preoperative Preparation

In addition to the usual preparation of the patient the following procedures may be mentioned:

(1) A Levin tube is inserted intranasally on the morning of operation. The end of this is kept at a level just proximal to the growth, and during the course of the operation constant suction is applied. This tube is then left in place above the level of the anastomosis during the first few days of convalescence.

(2) It will be obvious to anyone familiar with the technic of modern thoracic surgery that the induction of artificial pneumothorax as a preliminary to operation is unnecessary and undesirable.

(3) In depleted patients, starved by their inability to swallow, the performance of a preliminary jejunostomy may be advisable. If the state of nutrition is reasonably good, it is unnecessary. Of the 11 patients upon whom a resection with an esophagogastric anastomosis was performed, a preliminary jejunostomy was considered necessary in three. Seven cases in this series were successfully done without a jejunostomy.

Technic of Operation

The patient is placed on his right side with his left arm drawn upward. A long oblique incision is made over the course of the ninth rib (Fig. 6). The latissimus dorsi, trapezius, and a few fibers of the serratus anterior

muscles and a part of the lumbodorsal fascia are of necessity divided. The incision may be carried through the eighth or ninth intercostal space or through the periosteal bed of the resected ninth rib, according to individual preference. The intercostal incision can be made more rapidly, but is more difficult to close unless one relies entirely on large pericostal sutures. The rib resection technic requires more time with the opening, but provides an easier and more accurate closure. The incision must be long and the rib is

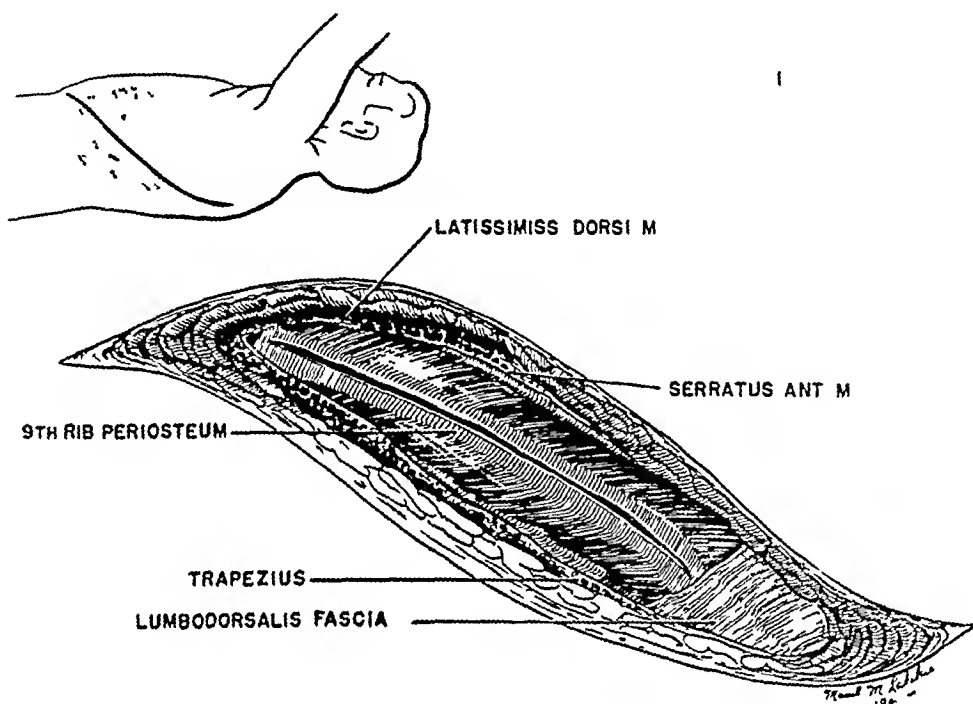


FIG 6—Transthoracic approach to the stomach—details and location of incision

resected from the cartilage to its articulation with the transverse process. In order to gain more exposure adjacent ribs may be divided posteriorly. It is well to avoid resecting or dividing the tenth rib, upon which the stability of the lower part of the thoracic cage depends. The necessity for cutting the costochondral arch is the chief objection to the combined abdominothoracic incision. Special rib retractors may be used if available, but two Balfour self-retaining abdominal retractors, one in each end of the wound, will serve very well. Although they have been omitted in the illustrations, large gauze pads are used to protect the wound edges.

The anatomy of the field of operation will be appreciated from a study of Figure 7. If the lung is adherent, it is separated by sharp dissection. After retracting the lung, the phrenic nerve is injected with novocain to immobilize the diaphragm. If resection is carried out, the phrenic nerve is crushed to maintain the immobility of the diaphragm during the postoperative period.

An incision is made through the diaphragm extending from its costal attachments to the esophageal hiatus. If a resection is decided upon, the incision is extended to divide the hiatus. In doing this the left inferior phrenic vessels on the undersurface of the diaphragm are ligated and divided.

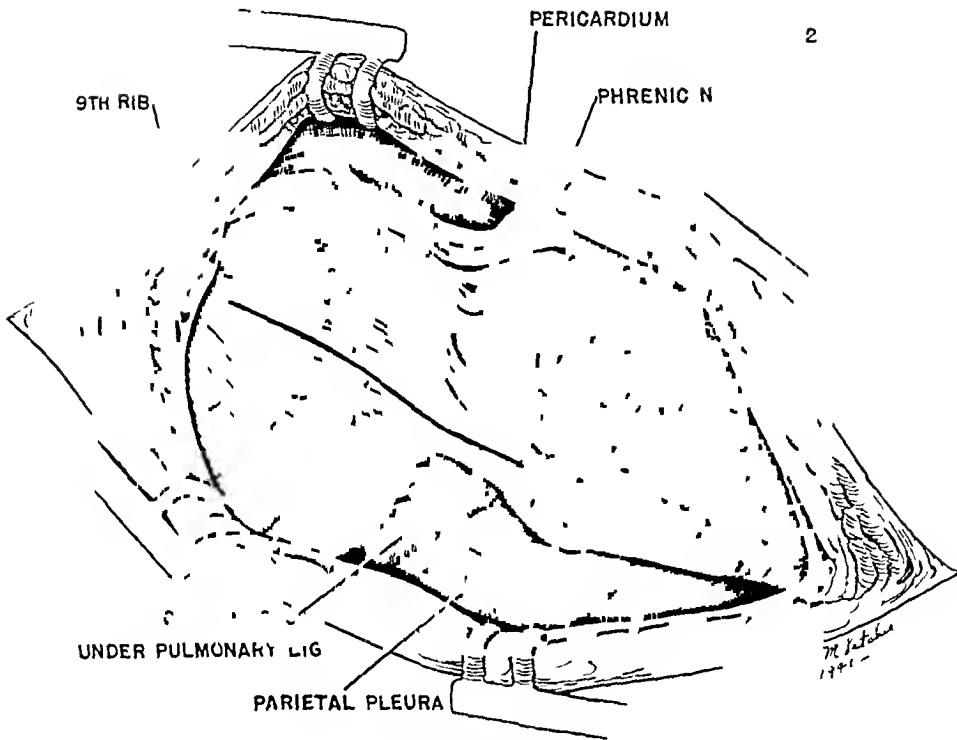


FIG 7—Transthoracic approach to the stomach—anatomy of the field of operation before incision of the diaphragm

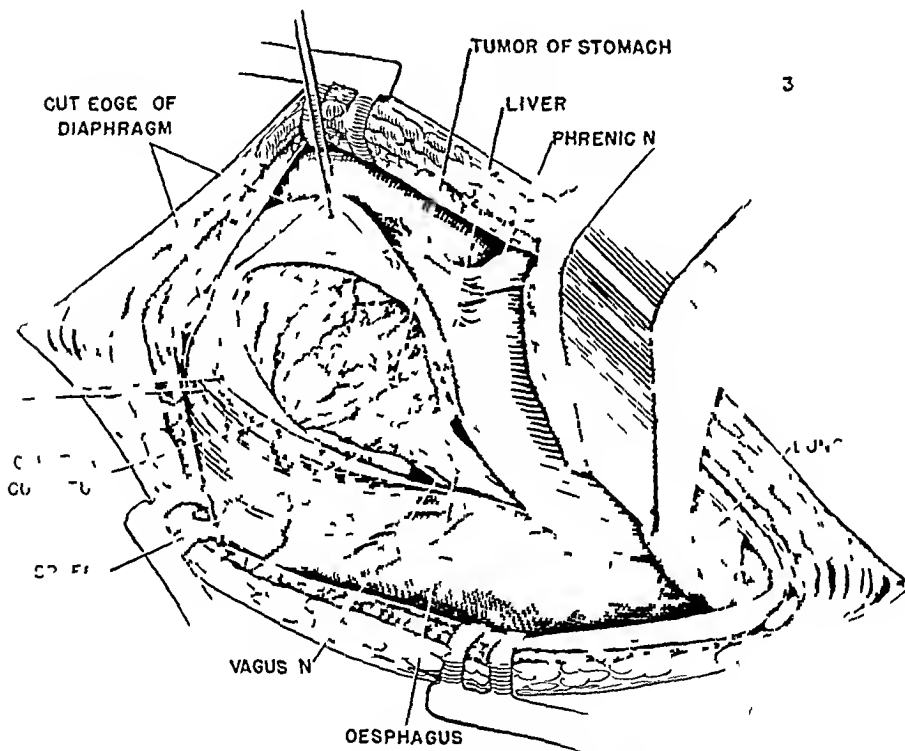


FIG 8—Transthoracic approach to the stomach—anatomy of the field of operation after incision of the diaphragm

It is at this point that one begins to realize the superiority of the trans-thoracic approach over that through the abdomen. The tumor, the anterior and posterior surfaces of the stomach, the retrogastric space, the retroperitoneal lymph nodes, and those in the upper portions of the gastocolic and gastrohepatic ligaments are directly accessible. Palpation of the liver is easily performed and in every case it has been possible to explore with the hand the entire abdomen, including the pelvic cavity, to feel for metastases.

If a resection can be performed, the phrenic nerve is crushed and the incision through the diaphragm completed. Long traction-sutures passed through the cut edges of the diaphragm and brought out through the wound are useful (Fig. 8). The spleen is held out of the way with a gauze pack. The liver is held back with a long flat retractor. The pulmonary ligament is incised and the lower two or three inches of esophagus mobilized.

The fundus and cardiac end of the stomach are mobilized by dividing the left gastric vessels and the vasa brevia. Vessels passing behind the cardia and the lower esophagus to anastomose with the inferior phrenic vessels are divided. Division of the vasa brevia and liberation of the upper pole of the spleen from extension of the growth into the lienorenal ligament is readily accomplished. Close adhesion of the upper pole of the spleen to the growth is an indication for its removal without attempting separation.

The left gastric artery may be divided at its origin in order to remove the regional nodes which surround it. The splenic artery is isolated at the point of its emergence on the upper border of the tail of the pancreas, and the posterior peritoneal wall of the lesser omental cavity at this point excised if the growth lies adjacent. Extension of the carcinoma to surround the splenic artery at this point may require its resection followed by splenectomy. Further extension to the tail of the pancreas is managed by partial resection of this organ.

At this point the field of operation is protected with a second set of gauze pads and care is taken to cover the intra-abdominal and intrathoracic surfaces as completely as possible. Whatever method is used to minimize contamination from the lumen of the esophagus, care is taken not to crush or devitalize it. A rubber-covered clamp may be applied loosely, a lung hilum tourniquet fitted with a broad tape may be used, or if suction by the indwelling tube is effective, no occluding device whatsoever need be applied. The esophagus is divided well above the highest level of visible or palpable tumor, but always at least two or three inches above the cardiac orifice.

Because of the strictly segmental distribution of its blood supply, the mobilization of the lower esophagus is done gently to avoid damage to the esophageal arteries which arise from the aorta. The esophagus is divided at least two or three inches above the cardia because the interruption of the left gastric, the vasa brevia, and the inferior phrenic arteries, all of which contribute to the blood supply to its lower extremity, may deprive the segment just above the cardia of an adequate circulation.

The stomach is divided below the level of the growth, placing the clamp

so that as much as possible of the greater curvature is preserved. The stump of the stomach is completely closed by suture. An end-to-side anastomosis between the esophagus and stomach is then performed (Fig 9)

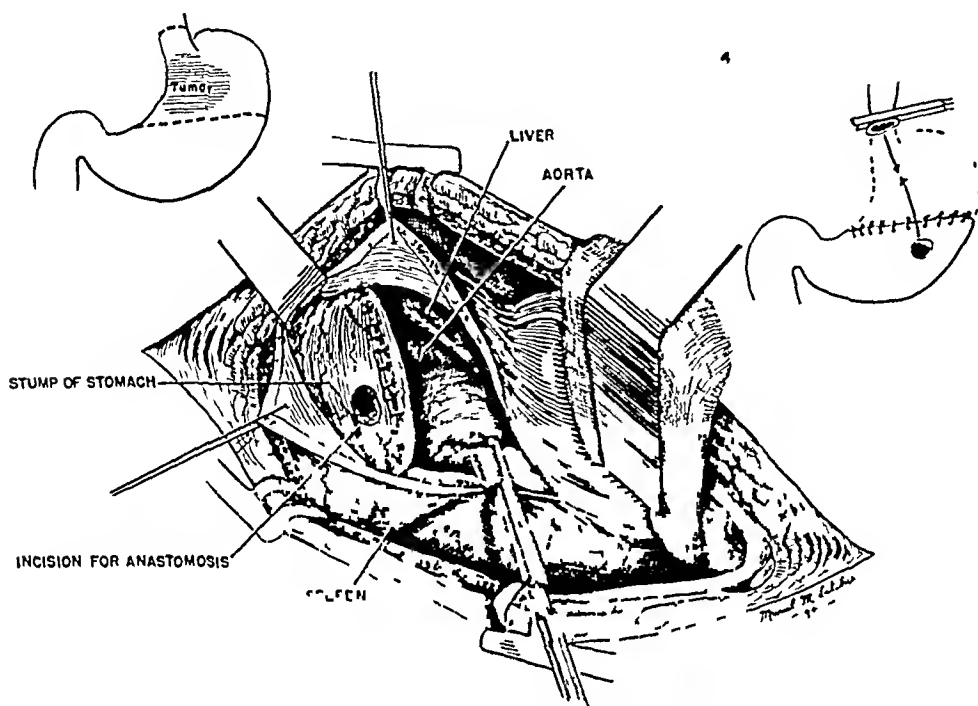


FIG 9—Transthoracic approach to the stomach—appearance after removal of the growth and closure of the cut end of the remaining portion of the stomach preparation for the anastomosis

Certain differences between this anastomosis and other gastro-intestinal anastomoses are important in determining the details of technic. Not only the tensile strength but the water-tight quality of the anastomosis depends on the row of sutures in the mucous membrane. This layer is sutured with the care and nicety accorded the placement of a vermilion border suture in the lip in the most meticulous plastic operation. Interrupted sutures of fine silk are used throughout.

To avoid any clouding of the field with blood while placing sutures in the mucous membrane, it has been found advantageous first to complete the preparation of the gastric part of the stoma. This is done before the stomach is anchored in position for the actual anastomosis. Certain authors report that a stricture is likely to result if a linear incision in the stomach is used. This objection is said to be overcome by excising a circular button from the stomach wall in forming the stoma. Both methods have been employed in our cases without discernible difference.

The sequence of the subsequent steps in performing the anastomosis is a detail which may be altered according to individual preference or the presenting complexities of regional anatomy. These steps are recorded in the classical sequence of gastro-intestinal anastomosis.

After complete hemostasis has been secured in the gastric incision made

for the anastomosis, the stomach is anchored high on the posterior thoracic wall to relieve tension on the suture line. Interrupted mattress sutures unite the posterior muscular layer of the esophagus to the serosa and muscles of

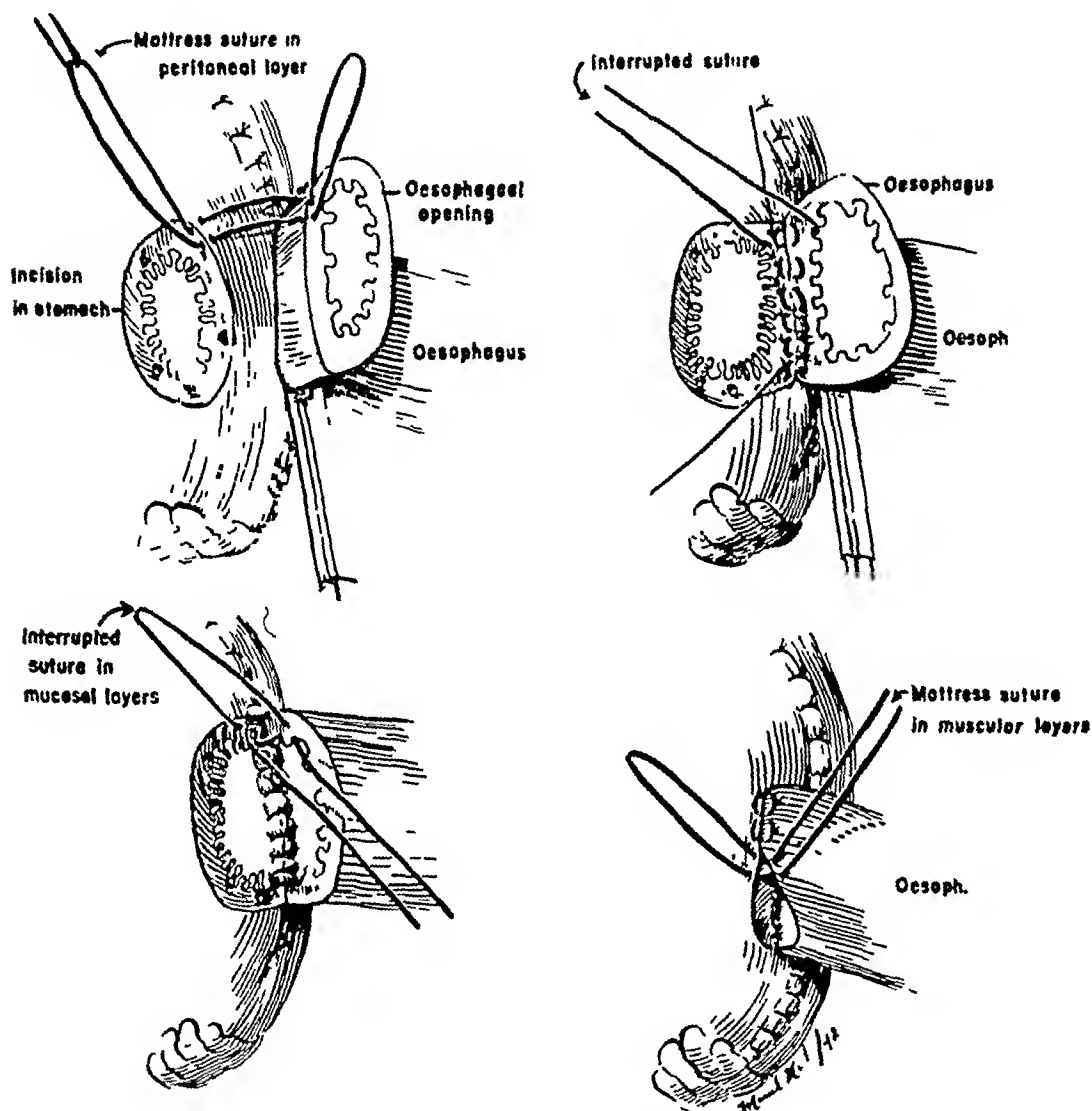


FIG 10—Transthoracic approach to the stomach—details of the esophagogastric anastomosis

the stomach. The mucous membranes are approximated with sutures so placed that the knot lies within the lumen. These are tied without tension which will lead to cutting when the tissues swell. An anterior row of sutures completes the union of the muscular coat to the stomach. The suture line is covered with omentum (Fig 10).

Certain measures are employed to make certain that the suture line is relieved from any tension. The leaves of the pulmonary ligament and adjacent mediastinal pleura are sutured to the stomach close to the suture line. The cut edges of the diaphragm are sutured to the stomach wall several centimeters below the level of the anastomosis. The remainder of the diaphragmatic incision is then closed. The thoracic wall incision is closed in layers (Fig 11).

During the course of the operation the left lung is kept partially collapsed,

but it is important at intervals of 15 to 20 minutes to allow the anesthetist to expand the lung fully for a few moments. At the completion of the operation, while the first layer of pleural sutures is being inserted, the anesthetist begins to expand the lung again, and before the last suture of the first layer is tied, the surgeon makes certain that expansion is complete.

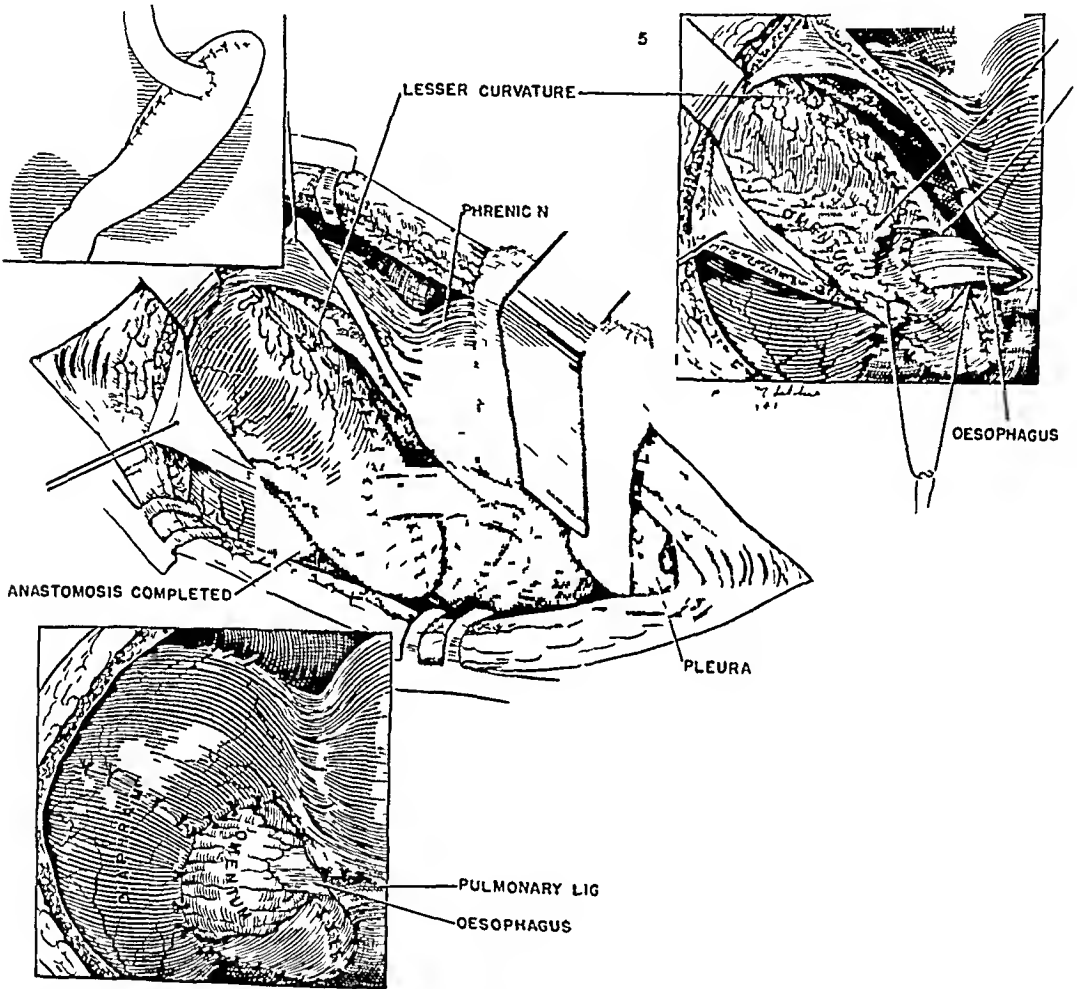


FIG. 11.—Transthoracic approach to the stomach—completion of esophagogastric anastomosis. Inserts show details of fastening omentum around the suture line and the methods of fixation of the stomach to avoid tension: suture to the chest wall, the leaves of the pulmonary ligament, and the paralyzed diaphragm.

Postoperative Care

Except for the incision and the conduct of the anesthesia, the operation itself differs little from any abdominal operation. The after-care, however, is practically entirely a thoracic problem, except for the usual considerations attendant upon the management of a gastric anastomosis. The patient is immediately placed in an oxygen tent or hood. Special nurses are essential. The usual transfusion and parenteral fluids are given. Suction is maintained on the intranasal catheter. This will usually drain a bloody fluid at first, but later, during the first few days, several hundred cubic centimeters of bile and gastric secretions may be aspirated. The lower end of this tube is kept

at a point just above the anastomosis. Fluids by mouth may be started in a week. The nasal tube is then removed. A soft solid diet is given by the end of two weeks.

Postoperative Complications

(1) Auricular flutter occurred in two cases. One of these (Case 16) recovered, the other (Case 13) died on the fifth postoperative day.

(2) Three patients developed empyema (excluding the two fatal total gastrectomy cases, both of which died because of sepsis). These were Cases 2, 5 and 14. In one of these (Case 2) the complication was serious and developed because of leakage from the anastomosis which was done by the now discarded method of implantation of the end of the esophagus into the stomach. The others were of minor importance and responded promptly to drainage.

Physiologic Considerations

(1) *Action of the Diaphragm* (a) In those cases where only an exploration is possible, preservation of the function of the diaphragm is undoubtedly preferable. In the cases with resection an inactive diaphragm is believed to be advisable to prevent pull on the sutures of the anastomosis. In this series no ill effects attributed to the paralyzed diaphragm were observed.

(b) Herniation through the diaphragm has been a complication in experimental animals, and in dogs has been a cause of vomiting. It can be successfully operated upon, as was shown by Adams and associates.³ There are apparently no reports of its occurrence in man.

(c) Pain referred along the course of the phrenic nerve to the left shoulder has not been observed even in the inoperable cases where the nerve has been preserved.

(2) *Gastro-intestinal Motility and Digestive Function* The possible harmful effects of dividing the vagus nerves must be considered. In some of the dogs described by Adams and associates, although they survived the operation, a slow death from inanition occurred which was attributed to loss of the vagus function. One of the patients in this series developed a severe nutritional deficiency characterized by all the signs characteristic of vitamin B-complex deficiency and nutritional edema. This occurred in spite of feedings by jejunostomy, parenteral administration of vitamin concentrates and liver extract, and transfusions. Although there was a complicating empyema, the nutritional deficiency appeared to have contributed in a large measure to the patient's death about three months after the operation. This has not occurred, however, in any of the other patients who have had a resection and esophagogastricostomy nor in two others on whom an esophagectomy for carcinoma was performed, at which time both vagi were cut. These patients maintain a good state of nutrition.

Fluoroscopic observation of the stomach after this operation reveals a diminished or absent gastric motility, but that of the duodenum and jejunum seems to be approximately normal. As would be expected also, there is

spasm of the pyloric sphincter. Careful anatomic studies, published by G A G Mitchell,⁴ would lead one to expect an overactivity (or rather an unopposed action) of the sympathetic nerve fibers that remain in the region of the pylorus and lower portion of the stomach.

Careful fluoroscopic observation of one of these patients (Case 6) whose lower esophageal stump and the fundus of the stomach were brought over the lower ribs and out through a subcutaneous tract, confirmed these expectations. In this case the gastric peristalsis was so weak and the pyloric sphincter so overactive that it was necessary to perform a pyloroplasty by the Hiencke-Mikulicz technic so as to inactivate and widen the pyloric sphincter. The details of a study of this case are to be published elsewhere.

As a result of this disturbance of gastric motility and hypertonicity of the pylorus, several of the patients upon whom an esophagogastric anastomosis has been performed complain of more or less difficulty of an obstructive nature for a few weeks after operation. This often leads them to believe that they are unable to swallow and may mislead their medical attendants to believe that they have an early recurrence. Fluoroscopic observation demonstrates that the delay is at the pylorus, not at the anastomosis. Experience has shown, however, that the condition is usually temporary and will correct itself.

A few patients complain of regurgitation of gastric contents into the esophagus, especially when lying flat. It has been relieved by elevation of the head of the bed or the use of more pillows.

TABLE III

TRANSTHORACIC APPROACH TO THE STOMACH (21 CASES)

Resection Followed by Esophagogastrostomy (11 Cases)

Case	Name	Age	Diagnosis	Result
(1)	H E	59	Carcinoma of cardia	Well 26 mos after operation
(2)	A P	59	Carcinoma of fundus	Died 3 mos after operation
(3)	J T	55	Carcinoma of fundus	Died with recurrence 14 mos after operation
(5)	P B	68	Carcinoma of cardia and fundus	Well 16 mos after operation
(9)	A D	67	Carcinoma of lower esophagus	Well 14 mos after operation
(11)	W E	49	Carcinoma of cardia and fundus	Well 11 mos after operation
(13)	O R	52	Carcinoma of cardia	Died in hospital
(14)	S M	44	Carcinoma of lower esophagus	Well 7 mos after operation
(15)	A K	64	Carcinoma of cardia	Well 7 mos after operation
(16)	J L	49	Carcinoma of cardia	Well 6 mos after operation
(19)	H C	50	Carcinoma of lower esophagus	Well 3 mos after operation

Total Gastrectomy with Esophagojejunostomy (2 Cases)

(10)	M O	55	Carcinoma of entire stomach	Died in hospital
(17)	G W	46	Carcinoma of cardia	Died in hospital

Total Gastrectomy in Two Stages (Inoperable at Second Stage) (1 Case)

(12)	W A	43	Carcinoma of entire stomach	Discharged from hospital
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Local Excision of Tumor (2 Cases)

(6)	E L	50	Sarcoma of fundus	Well 13 mos after operation
(21)	M S	36	Neurofibroma of cardia	Well 2 mos after operation

Exploration Only (5 Cases)

(4)	C W	40	Carcinoma of fundus	Discharged from hospital
(7)	F S	62	Carcinoma of fundus	Discharged from hospital
(8)	J O	72	Negative stomach	Discharged from hospital
(18)	L G	51	Carcinoma of fundus	Died in hospital
(20)	C E	36	Carcinoma of cardia and lower esophagus	Discharged from hospital

Summary of Experience with Carcinoma and Other Neoplastic Lesions of the Cardia and Lower Esophagus (Zone 3)

Table III shows that a total of 21 patients with lesions in this area were explored by the transthoracic route. Of these in one case no tumor was found. In four cases of carcinoma of the cardiac end of the stomach the growth was found to be inoperable. One of these remained in the hospital for terminal care and died four weeks after the operation. The other three were discharged two to three weeks after exploration. In a sixth case a two-stage transthoracic total gastrectomy was attempted, but the lesion was found to be inoperable at the second stage. There were two cases, one of neurofibroma and the other of fibrosarcoma of the fundus of the stomach, treated by local excision of the tumor through the transthoracic route. In the remaining 13 cases of carcinoma a resection was done. In two of these a total gastrectomy with an esophagojejunal anastomosis in the thorax was done. Both died, one because of leakage at the suture line, the other of widespread sepsis from soiling at operation but with an intact suture line. In the remaining 11 cases a resection and esophagogastric anastomosis was performed. In three of these cases the growth was in the lower end of the esophagus, in eight it arose in the stomach. There was one postoperative death (from auricular flutter). Ten patients survived the operation. Two of these have died of recurrent disease. All of the remainder are well and free from symptoms from three months to two and one-half years after the operation. These results may be said to compare favorably with those from resections for carcinoma in other locations in the stomach.

Note: Case histories to accompany this paper will be published in the October issue of ANNALS OF SURGERY.

REFERENCES

The extensive literature on the subject, as well as personal communications from many surgeons, has been freely utilized in attempting to resolve the maze of technical details that form the subject of this communication. Rather than to risk error by ascribing a source for specific ideas, we prefer to present the material as a recital of personal experience, completely disclaiming any originality of concept or methods.

- ¹ Sweet, R. H. Gastrostomy in Cases of Carcinoma of the Esophagus. *Surg., Gynec., and Obstet.*, 73, 55-62, 1941.
- ² Torek, F. The First Successful Resection of the Thoracic Portion of the Esophagus. *J. A. M. A.*, 60, 1533, 1913.
- ³ Adams, W. E., Escudero, L., Aronsohn, H. G., and Shaw, M. M. Resection of the Thoracic Esophagus, Experimental and Clinical Study. *Jour. Thoracic Surg.*, 7, 605-620, 1938.
- ⁴ Mitchell, G. A. G. Nerve Supply of Gastro-Esophageal Junction. *Brit. Jour. Surg.*, 26, 333-345, 1938.

DISCUSSION—DR. DALLAS B. PHEMISTER (Chicago): These results of Doctor Sweet's and Doctor Churchill's are perhaps the best that have been reported and the series is large enough in itself to establish transthoracic resection as the best treatment for tumors in these locations.

I have had 12 cases in which resection was performed with eight immediate survivals. In 12 cases the carcinoma was in the middle one-half of the esophagus and the

tumor was removed through the left chest and neck. Four cases survived the operation. One died, after four or five days of infection. Two cases subsequently died of the recurrences. Two are still free from recurrence, one, for over three months, and one, for 16 months.

In seven cases, the carcinoma was located lower down, three, in the esophagus, and four, in the proximal stomach. Resection was performed followed by anastomosis.

Four cases survived the immediate operation. One died of leakage and infection at the end of a week, one, of fibrillation and heart failure, and one of pneumonia and mediastinitis, without leakage.

Three cases are alive and apparently free from recurrence, one for nine months, one for 14 months, and one for four and one-quarter years. The last case was reported by Doctor Adams and myself, it the longest survival that I can find. This patient had carcinoma of the lower esophagus with metastases in the lymph nodes, in the upper portion of the lesser curvature, and it demonstrates that metastases in this region are not necessarily a contraindication to operation.

The 12 cases have been operated upon in one stage with one exception where a preliminary gastrostomy was performed. I believe that the routine should be a one-stage operation through the left chest. In the stomach cases, when the resection is extensive there may be difficulty of approximation for anastomosis. In one such case I incised the peritoneum alongside the duodenum and mobilized it so that anastomosis then became possible.

As to the technic in the highest esophageal cases where anastomosis is impossible. The left chest and the upper abdomen are prepared and draped in the same field. If the esophageal tumor after opening the chest, appears to be resectable, the lymph nodes of the upper part of the lesser curvature are then explored for metastases and the possibility of their operative removal. In one such case we found them involved and removed them. The esophagus is then freed in its entire extent and divided below the level of the tumor. If the lower end of the esophagus is long enough, the stomach is mobilized in its upper portion, a stab incision is made below and to the left of the xiphoid, and the esophageal stump is then pulled through. That procedure can be carried out very quickly. It has been employed in three cases.

If the stump is too short, a large mushroom catheter may be inserted, transthoracically, into the stomach and pulled through an anterior stab incision. The chest is then closed, the neck is draped, and the esophagus brought out through a neck incision after which the tumor is resected and the esophagostomy established either through a lower incision or if it is too short, through the same incision.

The thoracic duct was involved by the tumor in two cases, once within the abdomen and once up near the thoracic arch. It was ligated, divided, resected, and there was no leakage of lymph afterward. The left lobe of the liver was attached to the tumor in one case, and it was resected.

I want to show some malleable retractors for use in these resections. (Slide) This is for the lower resections when anastomosis is made. It is roughly a cross-section of the chest at that level. (Slide) Here is a malleable retractor for resection higher up. We have two or three for use according to the level of the tumor.

DR. WALTMAN WALTERS (Rochester, Minn.) I should like to make a few comments on one case of this type which I have done, paying tribute to Doctor Phemister and his associate, Doctor Adams, and to Doctor Ochsner and Doctor DeBaKey, for their excellent description of the technic of the operation.

I regret to say that I am not a thoracic surgeon, and that is one of the reasons I am reporting this case in view of the fact that, as a general surgeon the transthoracic removal of a carcinoma of the upper part of the esophagus did not seem to be such a difficult procedure.

I will not go into the details of the case, except to say that I followed exactly, as best I could, the description which Doctor Ochsner and Doctor DeBaKey described in their summary of their results in cases of this type. I believe that I learned a great deal from the case. For example, in Doctor Churchill's and Doctor Sweet's drawings, you will remember that the lower part of the esophagus seemed to be on a curve at its entrance to the anterior wall of the stomach. I believe that in the ensuing dilatations of the anastomoses which were necessary in the case I did, if you do not have that curve but

have a direct line between the esophagus and the anterior wall of the stomach, it will be much easier to carry out the dilatations

Secondly, I believe that Doctor Ochsner's use of the upper part of the stomach—that is the greater curvature—as an anchor, so to speak, as well as a tab, to protect the posterior part of the anastomosis and relieve the tension on it, is a very valuable procedure. I do not think it was illustrated in Doctor Churchill's and Doctor Sweet's drawings, but possibly they employed the same method. It relieves the tension on the anastomosis and then, with the use of the omentum around it anteriorly, it is very helpful in contributing to the blood supply of this area.

Finally, I believe that at least in my very limited experience, the skill of the anesthetist contributed to this patient's survival of a long operative procedure. You will recall, I said it was not difficult, but most certainly it was long. It took two hours and one-half to complete this procedure, and, at the suggestion of the anesthetist, every few minutes we would allow him to inflate the lung, cyclopropane being used. Then the loss of heat was prevented as well as one could possibly do so, with the use of moist gauze dressings. Multiple transfusions were used in this case, both preceding the operation and afterward. A one-stage jejunostomy was performed at the first operation. I did not know enough to ligate the gastrohepatic omentum or the ligamentum gastrolienale and its blood vessels at the time of the preliminary operation, which probably would have made the mobilization of the stomach much easier. But I was trying to feel my way along and failed to do it. Yet I found in the second stage that it had not particularly made the operation more difficult. In other words, I am only presenting this case because it may give encouragement to some of the surgeons who are less experienced in intrathoracic surgery and physiology.

DR ALTON OCHSNER (New Orleans, La.) A few words about the technical details. I am one of the advocates of the right-sided approach, primarily, because I think it is easier to do, and also because I have recently been able to demonstrate that one can remove all of the distal portion of the esophagus. I am talking about those cases in the resection of the mid-portion of the esophagus.

At the last meeting of the American Society for Thoracic Surgery, held in Toronto last June, the criticism was brought up that from the right side one could not remove enough of the distal portion of the esophagus. Since that meeting, I have had an opportunity to explore one of the patients upon whom we had operated from the right side. In reconstructing the esophagus anterior to the thorax, we brought up the stomach and found the entire esophagus had been removed and only the fundus of the stomach was left. So I think that it is possible to remove all of the esophagus from the right side.

Another technical point is that, in contradistinction to what Doctor Phemister does, we feel that the tumor should be removed in the chest and that it should not be brought up through the neck because of the danger of a possible implant from the tumor.

A word about the combined abdominothoracic tumor—those tumors located lower down. We feel that they should be undertaken in two stages, in contradistinction to the midportion of the esophagus—at the first stage not only determining whether the case is operable or not, but freely mobilizing the stomach, as Doctor Walters has mentioned.

In one of our patients the tumor had extended down to the lesser curvature. The case seemed inoperable. We mobilized all the gastrohepatic omentum, freed it down the greater curvature for about half the distance, and were able to remove all of the lesser curvature. That patient is alive now two years later. Had it not been for the fact that we had mobilized the stomach before, I am sure that it would not have been possible to have accomplished as radical a resection as we were able to perform.

DR EDWARD D. CHURCHILL (Boston, Mass., closing) I hope that the members of the Association will be willing to reserve their judgment in this field until those who are working in it have had a longer chance to solve some of these difficult problems. I think that it is a maze of conflicting details at the moment.

I think there are two or three fundamental principles that we must keep in mind in approaching any one individual patient. First of all, our goal is the cure of cancer, and we know from bitter experience in other fields, that any concessions made to future reconstructive plastic procedures may be pitfalls.

Second, we are doing our best to avoid intolerable mutilation under the excuse of palliation. I think the figures that Doctor Sweet showed were that approximately 50

per cent of the patients with the midportion of the thoracic esophagus involved which seem operable thoracically, have extensive abdominal lymph node metastases and in those cases, rather than subject them to the mutilating procedure we 'call it a day' and quit.

In the technical details there is no limit to the points of controversy and discussion. I should emphasize what Doctor Sweet said about the suture line in the esophageal gastric anastomosis which is on a different principle than the suture line of the gastro-enterostomy because the water-tight suture line and nearly all of the tensile strength of that suture line depend on accurate mucous membrane approximation and those mucous membrane sutures are placed with the exactitude and with the degree of tension that we would use in the fine plastic procedure on the lip. There must be no tension and there must be accuracy.

Doctor Ochsner and Doctor Sweet are on different sides in regard to the method of approach. While Doctor Ochsner points out that the entire esophagus can be removed from the right thorax I wonder if he would also say that the left gastric artery can be ligated at its point of origin and resected with the lymph nodes that run between that point and the cardiac end of the stomach.

I do not agree with Doctor Ochsner's comment that preceding abdominal operation, it is necessary to mobilize the stomach when you are contemplating performing an esophagogastric anastomosis, because we find that the exposure through the diaphragm is adequate to carry out a complete total gastrectomy should the occasion necessitate.

I will also point out that the surgeon may approach a patient, expecting to do a resection, with an esophageal gastric anastomosis and that he will find, by the time that he has gone far enough down on the stomach to give him a safe margin and far enough up on the esophagus to give him a safe margin he cannot bring the two ends together and he must convert his procedure to the turn-out operation.

DR RICHARD H. SWEET (closing) There are just one or two notes I made during the discussion that I would like to point out. As Doctor Churchill said in two cases we have converted a planned esophageal gastric anastomosis into a turn-out operation and have done essentially Doctor Phemister's one-stage operation.

I am sorry to hear Doctor Walters say that these cases should be undertaken only by thoracic surgeons. Or did I make the wrong inference? I think they should be done by abdominal surgeons because although I am told that many thoracic surgeons are excellent abdominal surgeons I know that the abdominal surgeons can make a most satisfactory anastomosis and I think the anastomosis is the most important part of the operation.

We have had no strictures in our cases. Just why, I do not know, but it remains as a fact. Perhaps we have paid unusual attention to the detail of the anastomosis.

THE PROBLEM OF INTESTINAL GASES COMPLICATING ABDOMINAL SURGERY*

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TO THE EXPERIENCED SURGEON gaseous distention before or following abdominal surgery is an unwelcome sign and so often indicates a serious condition it cannot be regarded lightly. At the same time a flat abdomen during convalescence is extremely comforting. Fortunately at this time, with better knowledge of its etiology, this complication is often preventable. Only those who practiced surgery 20 years ago, when gas formation was too little understood, can appreciate the importance of experimental physiologic studies of intestinal gases, and then origin, to the safety of abdominal surgery. To appreciate the serious problem of gaseous distention and the erroneous conception concerning its cause, and the methods employed for its relief, the younger surgeon should read the older text books,¹ which devote many pages under the headings of "Postoperative intestinal distention," "Acute postoperative intestinal obstruction," "Acute postoperative gastric dilatation," "Preoperative purgation, postoperative purgatives," "Mouth laxatives or mild purgatives" (such as calomel and soda), "Medicated rectal enemata." Turpentine stupes, poultices, icebags, strychnine, physostigmine and atropine were commonly used. Each surgeon had his especial enema containing various drugs. One famous surgeon of the South had an enema of renown which was called "16 to 1 enema" after the W. J. Bryan money-standard-plan of 16 parts of silver to one of gold. This enema had 16 drugs to one part of water, and no gas could resist it.

The erroneous belief that intestinal gases were the result of putrefaction caused preoperative purgation and starvation to be practiced, routinely, to prevent postoperative distention. It was a long time before it was realized that such practices, far from preventing distention, actually increased and prolonged distention and delayed the return of peristalsis. Furthermore, the resulting disturbance of water and electrolytic balance was at times so great as to bring about death of the patient. Although it was early noticed by some workers that cases which were operated upon as emergencies without preoperative preparation, had less distention than those who were extensively prepared in advance, nevertheless, there seems to have been no implication that the purging and starvation policies were actually at fault.

What are the Effects of Gaseous Distention? Gatch² has stated that "Distention is the most important cause of death from all forms of bowel obstruction, mechanical or paralytic, and most of the other supposed and suggested causes of death cannot exist in the absence of distention." With this statement we agree. Since distention does play such a vital rôle in

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abdominal surgery, it might be well to consider first of all the specific effects which it produces

Effects of Gaseous Distention—Toxic Effects There is very little support for the theory, largely originated by Amussat,³ that with accumulation of gases and liquid material in the intestines toxic products are absorbed into the general circulation. Some workers contend that liquid or gaseous contents of the bowel or other harmful products as undigested protein and bacterial toxins are absorbed, but these are not under normal conditions absorbed until they are broken down into nontoxic material.^{4, 5}

Effects of Impairment of Circulation of Bowel Wall from Gas Pressure Gatch, following extensive investigation, is of the opinion that the various effects of gaseous distention may be largely traced to the pressure upon the bowel wall, affecting its blood and lymphatic circulation. This pressure results in anemia of the bowel wall and, later, a congestion, which may seriously involve the viability of the wall. In addition, normal lymphatic capillary function may be seriously involved, with the loss of the selective power of absorption. "(1) By diminishing the volume of blood flow through the intestinal wall, (2) by altering the physical forces involved in absorption, and (3) by damage to the intestinal wall, this affects both the activity of the mucosa and the physical forces which hinder or promote absorption."

Effect of Distention on Intestinal Tone Not among the least important of the effects of distention is the interference with the normal motility of the bowel. With stretching of the tissue, decreased activity of the nerve mechanism of the bowel, as well as of the muscular contraction, results, and if the distention lasts for a considerable length of time, even though the distention is relieved, the power of contraction is delayed, often for several days, resulting in what is known as "paralytic ileus." Abnormal distention of all hollow organs, if prolonged, results in atony. This is commonly seen with the urinary bladder. Again, sudden overdilatation of the stomach may result in "acute dilatation" with a loss of contracting power. The overdistended intestine behaves in a similar manner. Also the temporary ileus which accompanies trauma to the bowel will be prolonged if the bowel is distended but if the bowel remains collapsed normal peristalsis is sooner restored. If this is true, keeping the bowel free of gas is indicated after trauma to the bowel (operation).

Other Effects of Distention Less Easily Explained may be (1) *Changes in blood concentration* have been reported by Fine and coworkers, and also Gatch and Battersby, who observed that intraperitoneal loss of blood protein results from distention, and blood concentration follows. (2) *The effect of distention on liver and kidney function* has been indicated by Oll, and associates.⁶ They think that distention may play a part in the failure of liver and kidney function. "Liver function is first impaired by nerve reflex inhibition due to distention of the intestine. The anoxemia present in cases of severe intestinal distention may produce a marked impairment in the formation of bile and urine."

* Personal communication

Van Duyn II⁷ has concluded from careful clinical observation that abdominal distention may be the etiologic factor in blood changes similar to "*leukocytic exhaustion*" He found a mixed degenerative-regenerative picture with neutrophils, myelocytes, monocytopenia and absence of eosinophils He states "Abdominal distention is concluded to be at least one important cause of the degenerative blood picture The actual mechanism of production is through absorption from the distended intestinal wall of some apparently nonbacterial toxic substance which acts either directly or indirectly as an inhibition of leukopoieses "

ORIGIN OF INTESTINAL GASES

In order to prevent gaseous distention it is necessary to understand the origin of intestinal gases

As the Chief Source The origin of intestinal gases has been generally misunderstood for a long time, and the belief that intestinal gases originate within the bowel and are largely the result of putrefaction is firmly fixed in many minds Kantor⁸ said, in 1918, after animal experimentation, that "In general, gaseous accumulations in the upper digestive tract have atmospheric air as the base The air is introduced by swallowing " Again, Bickman,⁹ in 1924, wrote that postoperative distention was partly due to swallowed air

In spite of these early observations, surgeons have been slow to appreciate and accept the fact that swallowed air is by far the chief source of intestinal gases in normal intestines as well as the intestine in a condition of ileus or obstruction

In support of the theory that swallowed air is the chief source of intestinal gases, analyses of these gases have frequently been made, and the variations from the gases of the air have been found to be slight An analysis of the gases of the air is as follows

	Oxygen (O ₂)	Nitrogen (N ₂)	Carbon Dioxide (CO ₂)	Methane Hydrogen
Composition of air	20.96%	79%	0.4%	—

TABLE I

ANALYSES OF INTESTINAL GASES IN ANIMALS WITH ILEAL OBSTRUCTION

Singleton and Rogers

Analyses of Gases Withdrawn from Intestine of Mechanically Obstructed Dogs

Dog No	Hours	CO ₂ %	O ₂ %	N ₂ %	CH ₄ %
1	72	4.5	10.7	83.0	1.8
2	48	10.7	3.1	82.6	3.6
6	12	5.9	13.1	80.8	0.2
7	48	9.1	1.5	89.4	0.0
8	48	9.3	0.0	90.7	0.0
9	72	14.0	5.8	77.4	2.8
10	72	12.1	0.8	87.1	0.0
Average Composition Intestinal Gas		9.51	5.0	84.42	1.2
Composition of Atmospheric Air		0.04	20.94	79.02	0.0

Wangensteen's¹⁰ Report

N	Carbon Dioxide	O ₂	Methane Hydrogen	H ₂ S	Ammoniated Methane
70%	6-12% (near that found in blood gases)	10-12% (drop after 72 hours)	Low %	1-14% (increase after death)	1/2-4% (increased with long obstruction)

Wangensteen says "In quantitative determination of the origin of gases occurring in small bowel obstruction, about 68 per cent of the gas was estimated to have arisen from swallowed air. The amount formed within the body was 32 per cent of the amount, 70 per cent originated from diffusion from the blood into the bowel lumen, and the remaining 30 per cent arose from decomposition of food matter." In other words, only 9 per cent of the total was from decomposed matter.

Clinical Analysis of Intestinal Gas McIver, Benedict and Cline¹¹ analyzed gases drawn from the rectum in postoperative distended patients and nonsurgical patients. The percentage of nitrogen is uniformly high, and since free nitrogen is liberated in the intestine only in small quantities, if at all, it must be derived from air, either directly from swallowed air or indirectly from diffusion from the blood stream, which is saturated with nitrogen. The oxygen figures are low. The percentage of hydrogen and methane are lower in postoperative distention than in medical cases. Since the composition (except for the small amounts of hydrogen and methane) is that of air modified by interchange with the blood gases, the findings are not inconsistent with the view that swallowed air plays a rôle in the production of postoperative distention.

Wangensteen and Rea's¹² experiments with cervical esophagostomy not only proved conclusively that distention was due to swallowed air in obstruction but that distention hastens the death of the animal. He says "The exclusion of swallowed air obviates the distention factor and, in turn, the sequelae of decreased viability and increased permeability which attend sustained increases of intraluminal pressure—that the mechanical factor of distention and not a 'toxic factor' accounts for the lethal issue in ileal obstruction." We have repeated Wangenstein's esophagostomy experiments and found that no gas could be recovered from the obstructed intestine.

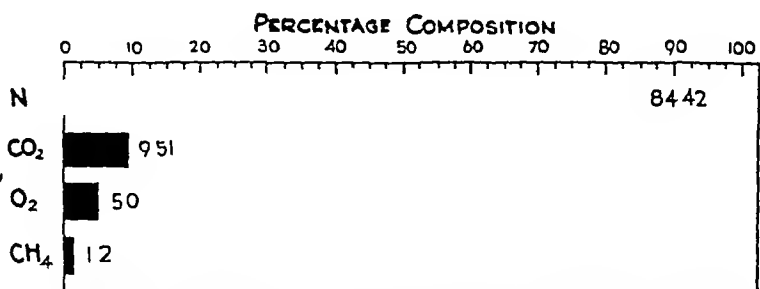
As further evidence that intestinal gases come from swallowed air we have observed that in patients with excision of the esophagus or with complete stricture, with gastrostomy feeding, the absence of gas in the bowel, even in the colon, is quite noticeable.

RELIEF OF DISTENTION

Unfortunately, distention has already occurred in many cases before the patient reaches the surgeon in intestinal obstruction or acute abdominal inflammatory diseases, such as cholecystitis, appendicitis, etc. in which case the problem of removing the gas is paramount. Enemata, purgatives, eserine, pituitrin and other drugs are generally not dependable and are better employed sparingly. The use of gastric or gastroduodenal suction may remove some of the gas from the intestine, but, more important, it will prevent further distention, and the absorption of some gas will occur, giving a degree of relief. After distention has occurred the problem of removing the gas is a difficult one either in dynamic or adynamic ileus, chiefly because the nitrogen is not absorbable.

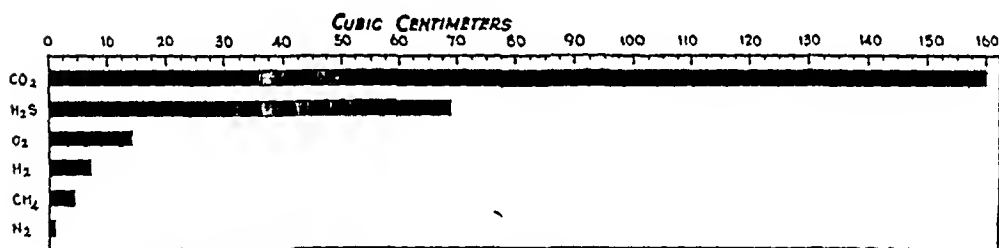
McIver, *et al*,¹³ found that the rates of absorption of intestinal gases varied

Nitrogen has a very low rate of absorption because the blood and tissues are saturated with N_2 (of an atmospheric pressure) Swallowed air is 79 per cent N_2 , and intestinal gases are 70 per cent N_2 Thus, we conclude that gaseous distention is largely the result of swallowed air, and we, further, see why distention is not relieved by the absorption of the intestinal gases



Average composition of intestinal gases of mechanically obstructed dogs -

CHART 1



Relative rates of absorption of intestinal gases (After McIver)

CHART 2

Furthermore, when the intestine becomes distended, resulting in venous stagnation, CO_2 , instead of being absorbed by the blood stream, as occurs normally, is diffused from the blood stream into the lumen of the bowel, thus increasing the distention

If no more air is allowed to enter the intestine, gastroduodenal suction, aided by reversed peristalsis, will remove a considerable amount of gas This was the experience of Wangenstein early in its use Some gas is absorbed by the blood stream and some observers have succeeded in increasing this absorption (nitrogen) by breathing a *high concentration of oxygen* Fine and Sears¹⁴ found by inflating a closed loop of bowel with N_2 and another loop with hydrogen, that nitrogen was absorbed from the intestine in small amounts if air was breathed If pure oxygen was breathed, the absorption was much more rapid They also observed that these gases were not absorbed from the stomach as rapidly as from the intestine

Congdon and Burges,¹⁵ as well as Binger, Faulkner and Moore,¹⁷ report experimental and clinical experiences to justify the use of concentrated oxygen in the relief of distention

Rosenfeld and Fine¹⁷ say "Breathing of 95 per cent O₂ results not only in a striking decrease in gas volume but also in a marked reduction in the pressure within the lumen of the intestine. The lethal effects of a sustained high-grade gaseous distention are thereby delayed or entirely avoided." They found that clinically, therefore, *pure* oxygen inhalation over periods of 12 to 24 hours reduces intestinal distention. Also, it was found that intermittent breathing of oxygen was almost as efficacious as continuous breathing of it (Though our experience is confined to only a few cases we have thought its use of some benefit.)

The giving of concentrated oxygen is not without danger, overdose may result in oxygen poisoning with pulmonary congestion, liver congestion and right heart failure (Paine, Keys and Lynn¹⁸).

The Miller-Abbott tube, in cases of intestinal obstruction, is quite useful and often life-saving, but there are frequently technical difficulties in passing the tube which has prevented universal success with its employment.

PREVENTION OF DISTENTION

Gastric Suction and Its Advantages—We wish in this paper to stress the importance of the *prevention of gaseous distention* rather than the relief of distention after it occurs. The recognition of the frequency of postoperative distention and the realization of the seriousness of distention as a complication, caused us to adopt the practice of using gastric suction routinely in all abdominally operated patients and we have continued this practice for the past five years. The result has been that postoperative distention is no longer encountered.

The problem of keeping air out of the intestines is a simple one. McIver¹¹ in 1926 used an indwelling tube in the stomach postoperatively to prevent distention, but said "Since it is occasionally a source of annoyance to the patient, its use indiscriminately is not advocated, but in certain cases in which distention is feared as a grave complication it should be employed."

The plan we have followed is as follows. A Levin tube† is put in place just before the anesthetic is started and allowed to function throughout the operation and until peristalsis has been restored. The tube is kept open by drinking water which the patient enjoys to the extent of tolerating the tube. In 24 to 48 hours the tube is clamped for three hours and the water which is taken by mouth is measured. The tube is then released and the returned fluid measured. If little of the fluid is recovered, it is felt that peristalsis has returned and the tube is removed. On the other hand, if all the fluid is returned suction is continued. In complicated cases such as peritonitis and

*In young children, with operation in the early stage of appendicitis, without peritonitis, we have not routinely used suction. The reflexes being more highly developed in the young, peristalsis is restored more readily and prolonged ileus rarely occurs.

†The tube should not be smaller than a No. 16 F. It is inserted just past the first mark, and must be kept open at all times.

intestinal, gastro-intestinal and gastric resections, suction is continued for a longer period of time. The average length of time for postoperative suction in common operations is as follows:

- (1) Uncomplicated appendicitis, 24 to 36 hours
- (2) Ruptured appendix with drainage, 48 to 72 hours
- (3) Cholecystitis, or cholecystectomy, 48 hours
- (4) Resection of stomach, 72 to 96 hours
- (5) Resection of cecum, 72 to 96 hours
- (6) Resection of rectum, 72 to 96 hours

We have made a clinical study of some 500 patients who had abdominal operations, upon whom gastric suction was employed, and compared them to a long list of patients with similar operations before gastric suction was practiced. While this study has been tedious and in many ways incomplete, the general conclusions drawn are to the effect that:

- (1) Gastric suction correctly used prevents *postoperative distention*
- (2) When the abdomen is opened the stomach is empty and collapsed, the advantage of this is evident
- (3) There is no postoperative vomiting
- (4) There is no distention, with the discomfort that goes with distention
- (5) Peristalsis is restored much sooner if the bowel is not distended, and if air is not allowed to pass into the intestine until the bowel recovers, distention does not occur
- (6) Wound healing is more satisfactory, with few postoperative herniae, and no disruption of wounds
- (7) There is a lowering of morbidity and of mortality

Disadvantages—There are disadvantages to gastroduodenal suction. The most serious criticism of *gastroduodenal* suction is the loss of fluids and electrolytes, in the form of bile, pancreatic juice, and chlorides from the stomach. From a careful study of the problem, we believe that a distinction should be made between *gastroduodenal* and *gastric* suction (Fig 1). In a series of

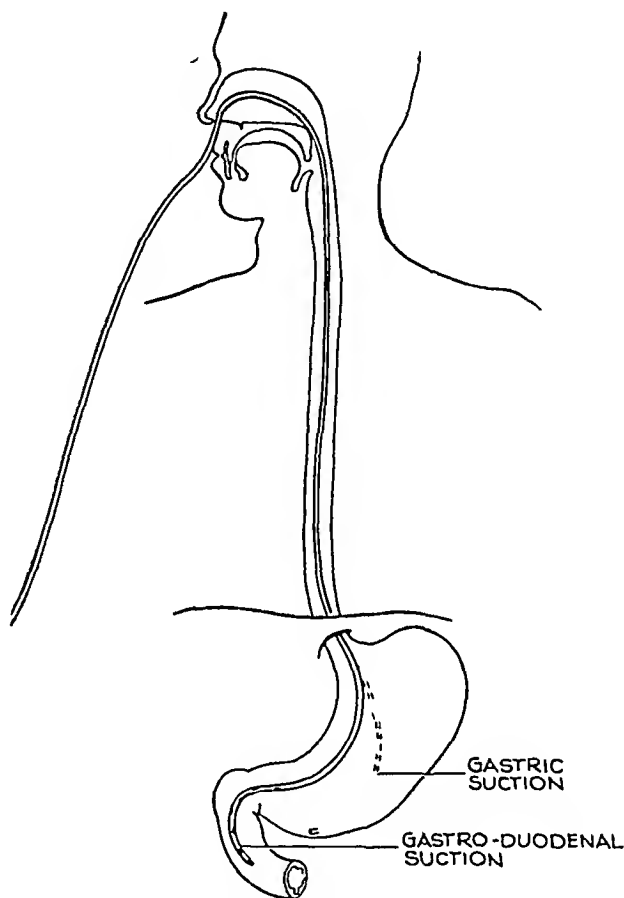


FIG 1—Gastric suction as distinguished from gastro duodenal suction

observations we found that the *fluid loss* by suction, when the tube extended into the duodenum, was considerably more than when the tube extended only into the stomach. With the tube in the stomach many patients showed little or no bile in the suction fluid. A careful check of a series of more than 75 patients showed that rather than a loss of fluid with gastric suction there was more often a gain during the period of suction with the patient drinking water freely (Table II).

TABLE II
STUDY OF FLUID LOST OR GAINED WITH GASTRIC SUCTION

Patient	Operation	No of Hours of Suction	Fluid Retained by Mouth	Fluid Lost	Average Amount of Fluid Lost or Retained in 24 Hours	
					Gained	Lost
Mrs S	Hysterectomy	58		-595 cc		-200 cc
Mrs W	Strang hernia	46	+850 cc		+425 cc	
S B	Cholecystectomy	48	+550 cc		+550 cc	
Mrs R	Ruptured <i>peptic</i> ulcer	75	+650 cc		+200 cc	
Mr R	Subphrenic abscess	46	+1 225 cc		+650 cc	
C T	Cecostomy	60	+2 006 cc		+600 cc	
Mr H	Gastro enterostomy	73	+1 275 cc		+400 cc	
Mrs R	Hysterectomy	44	+1 140 cc		+550 cc	
Mrs S	Appendicectomy	28		-950 cc		-900 cc
Mr K	Cholecystectomy	46	+1 050 cc		+500 cc	
Mrs A	Colostomy closed	66		-26 cc		-10 cc
F W	Strang hernia	25	+1 200 cc		+1 200 cc	
N V	Appendicectomy	24	+200 cc		+200 cc	
P F	Abscess Appendicectomy	30	+150 cc		+100 cc	
Mr W	Herniotomy	24	+1 200 cc		+1 200 cc	
B R	Appendicectomy	33	+575 cc		+450 cc	
Mrs H	Cholecystectomy	49	+2 000 cc		+1 000 cc	
A C	Ileostomy	52	+75 cc		+30 cc	
L C	Cholecystectomy	45		-1 195 cc		-550 cc
R M	Cholecystectomy	47	+2 000 cc		+1 000 cc	
Mr P	Gastro enterostomy	84	+2 500 cc		+600 cc	
M D	Cholecystectomy	42	+1 500 cc		+700 cc	
B C	Exp celiotomy	50	+680 cc		+300 cc	
Mrs R	Obstruction (ca) —Colostomy	50	+680 cc		+200 cc	
E T	Hysterectomy	28		-210 cc		-200 cc
E B	Appendicectomy	24		-800 cc		-800 cc
H H	Gallbladder drainage	72	+500 cc		+150 cc	
Mrs S	Appendicectomy— Peritonitis	48	+975 cc		+475 cc	
P L	Appendicectomy	28	+280 cc		+270 cc	
Mrs S	Exp celiotomy	32		-450 cc		-350 cc
Mrs H	Cholecystectomy	65		-925 cc		-350 cc
Mrs B	Cholecystectomy	91	+726 cc		+200 cc	
G L	Appendicectomy	26	+1 200 cc		+1 200 cc	
A E	Appendicectomy	43	+350 cc		+175 cc	
F K	Rectal resection	90	+2 100 cc		+500 cc	
C C	Gastric resection	55	+1 175 cc		+400 cc	
Mrs S	Cholecystectomy	46	+1 750 cc		+900 cc	
Mrs M	Cholecystectomy	50	+2 420 cc		+1 000 cc	
A A	Appendicectomy	18	+50 cc		+50 cc	
G A	Cholecystectomy	19	+1 000 cc		+1 000 cc	
J V	Drainage Appendicectomy	55	+1 500 cc		+700 cc	
M P	Colostomy closed	24	+1 500 cc		+700 cc	
M B	Appendicectomy	43	+2 000 cc		+1 000 cc	
A A	Colostomy Ca colon	64		-825 cc		-300 cc
W D	Stab wound	50		-750 cc		-300 cc
B S	Appendicectomy	37		-150 cc		-100 cc
H C	Intestinal resection	60		-515 cc		-200 cc
M H	Stomach resection	64		-2 500 cc		-900 cc

SUMMARY

Number of patients	50
Number gaining fluid	35
Number losing fluid	15
Maximum retained per 24 hours	1 200 cc
Minimum retained per 24 hours	50 cc
Average retained per 24 hours	562 cc
Maximum loss per 24 hours	900 cc
Minimum loss per 24 hours	10 cc
Average loss per 24 hours	370 cc

Loss of Chlorides—On the other hand, an analysis of the fluids recovered with gastric suction showed a definite and regular loss of chlorides as shown in Table III

TABLE III

AVERAGE SODIUM CHLORIDE LOSS PER 24 HOURS*

Patient	No of Days Suction	Urine Gm	Gastric Juice Gm	Total Gm
C M	4	6 41	7 77	14 18
E W	3	5 46	5 11	10 57
C M	4	2 28	2 07	4 35
L P	1	5 91	2 50	8 41
J M	3	4 76	4 50	9 26
W C	3	1 32	6 93	8 25
P H	3	5 59	4 67	10 26
A M	4	3 44	5 17	8 61
Mrs F	5	7 88	4 71	12 59
E M	2	4 60	1 57	6 17
F G	3	5 46	6 73	12 19
Total average		5 1	4 9	9 51

hours—9 81 Gm

* Patients had no stools nor appreciable amount of sweating during investigation

This loss corresponds quite accurately with the finding of Coller¹⁹ in his studies of chloride balance. He found that gastric suction removed the equivalent of 3.7 to 4.8 Gm of salt in 24 hours.

It is unnecessary to say that pre- and postoperative attention to fluid and electrolyte balance in accordance with the principles established by Coller,²⁰ and associates, is indispensable to abdominal surgery and they are of still greater importance when gastric suction is employed. This is particularly true in estimating the amount of sodium chloride to be given.

The annoyance of the tube to the patient is a problem, but the elimination of vomiting, gas pains, enemata, and the discomforts that accompany distention outweigh the discomfort from the tube.

Some reports of damage to the nasal cavity, pharynx, and larynx are found in the literature. We have not encountered any of these. In those cases where prolonged use of the tube is necessary, frequent changing of the tube will obviate this danger.

COMMENT AND SUMMARY

That postoperative distention is a serious complication will be admitted by all. The prevention of distention as a complication of abdominal surgical operations is easily accomplished. The intestinal gases are, for all practical

purposes, composed of swallowed air, and gastric suction, if efficiently employed, will recover this air. Large amounts of air is swallowed during the anesthesia and after the operation. When a patient is nauseated and has a disagreeable taste as is experienced during an anesthesia, and postoperatively, there is, naturally, frequent swallowing in the natural effort to fill the stomach to reflexly stimulate vomiting. Since the patient is in a reclining position, the opening of the esophagus into the stomach is in a dependent position and regurgitation of air does not occur.

Further, we are of the opinion that, if the suction tube does not pass into the duodenum, the loss of fluids (pancreatic juices and bile) will be much less but still the air will be recovered.

The value of this procedure is particularly noticeable in acute *inflammatory intra-abdominal* conditions, as well as in *intestinal obstruction*. Ileus is of little consequence in the absence of gaseous distention, and even in advanced peritonitis cases one can more safely wait for a favorable time for operation by using gastric suction and preventing further distention. It is also true that if the advanced peritonitis patient be operated upon, the prevention of distention following operation guarantees rest of the bowel, maintenance of good intestinal circulation, giving the protective power of the peritoneum much better chance to take care of the infection.

Another very striking occasion where we have found gastric suction indispensable is in the very large abdominal and diaphragmatic hernia in which the intestines have been outside the abdominal cavity for a long time, with a marked reduction in the size of the cavity. These patients were formerly great hazards or impossible operative risks. Forcing the hernial contents back in the abdominal cavity and closing the wound under tension is possible. Keeping the bowel deflated for several days until peristalsis is restored, makes this procedure safe without which a fatality would result.

In operations upon the stomach, intestines, colon or rectum, and more particularly where stomach and intestinal suturing is done, the value of eliminating distention for several days is readily apparent. Enterostomies proximal to anastomoses are no longer necessary. We can say, with all sincerity, that no one thing has contributed so much to the advancement of abdominal surgery in recent times as this simple procedure of keeping the bowel deflated.

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DISCUSSION—DR WILLIS D GATCH (Indianapolis, Ind) We are indebted to Doctor Singleton for calling to our attention this method of preventing postoperative distention. He is right in his contention that the distending gas is chiefly nitrogen derived from swallowed air. The results he reports convince us of the efficiency of his method. Since I can find no matter for controversy with the essayist, I shall devote my discussion to the amplification of some of the more theoretic points he has made.

Gastric distention is far more deadly than intestinal distention. If the pylorus of a dog is tied and its stomach inflated with a sustained pressure of 25 Mm it will die of asphyxia in two hours without concentration of the blood. Inflation of its stomach with a

sustained pressure of about 10 Mm will cause its death in about six hours and its blood will be considerably concentrated. It may survive a marked inflation of its small intestine for ten to 15 hours.

Patients, as Doctor Singleton has remarked, often swallow great quantities of air in the induction period of anesthesia. The resulting dilatation of the stomach offers a serious impediment to the respiration which I believe may be fatal in some cases. We have shown experimentally that distention of the stomach and of the intestine causes marked elevation and fixation of the diaphragm. When this is present the total amount of air which the animal breathes is increased five or six times over normal but despite this it becomes asphyxiated. When the capacity of the thorax is decreased by elevation of the diaphragm, the lungs are incapable of oxygenating the blood completely and this inability cannot be removed even by the administration of pure oxygen. It of course follows that anesthesia is made much safer by deflation of the stomach.

The essayist has discussed briefly the ill effects of bowel distention. The literature on this subject is vast and full of contradictory conclusions. We believe that most of these can be explained and reconciled by the primary conception that the essential effect of bowel distention is to increase the intercellular or tissue pressure in the bowel wall with results which are made easily comprehensible by Starling's hypothesis on the capillary circulation. The corollary to this conception is that there are two well-defined stages of bowel distention. Thus if a loop of intestine is inflated with a rather low pressure it will be found to have a diameter of about one inch. This diameter will remain constant as the pressure is increased up to the point at which rupture of the bowel occurs. If however a loop of intestine is tightly inflated and kept in the abdomen its diameter will gradually increase up to perhaps two to three times normal. If the pressure is measured in this distended intestine it will be found to be comparatively low—probably 10–15 Mm. The circulation in the tightly distended bowel is practically at a standstill. The bowel is pale, bloodless and no fluid collects in its lumen. The dilated bowel is blue, edematous and flaccid. We have shown that its cyanosis is due not to venous obstruction, but to vasomotor paralysis. Its circulation is present but in a crippled condition. An albuminous exudate collects in its lumen. Its power of absorption is greatly diminished and its walls have been stretched until they have lost the power to contract. The bowel is being injured in the first stage of distention; it is recovering from injury in the second stage. It passes from the first stage to the second stage when its wall stretches enough to lower the pressure to a level at which a continuous flow of blood through its capillaries can occur. Of course if the intra-intestinal pressure increases as the bowel dilates the second stage will not be found. Very few direct measurements of intra-intestinal pressure in man have been made. Those recorded vary from 111 to 13 Mm. It is interesting to note that Stone and Firor, who report the measurement of 111 Mm, state that the intestine was tightly distended.

When a bowel is found in Stage two of distention, relief of the mechanical cause of the obstruction will not relieve the obstruction for a period of days because the bowel has lost its power to contract.

Our experimental results have led us to believe that the concentration of the blood which occurs when the stomach or intestine is distended is due to asphyxia.

The essayist has referred unfavorably to the use of pitressin in the treatment of post-operative distention. Mann has shown that this drug is dangerous because it causes a great decrease of blood flow in the walls of the heart.

DR FREDERICK A COLLIER (Ann Arbor Mich.) I think we all agree with Doctor Singleton at least those of us who have done abdominal surgery that distention can be and very frequently is one of the most distressing and not infrequently fatal complications that can occur. I think many in this room can remember back to a time when we felt that this distention was due to fermentation and putrefaction and the only treatment we had was as Doctor Gatch has mentioned, cathartics and enemata of all kinds variously flavored. I remember one flavor we had was nutmeg. And of course we had the rectal tubes.

As far as I know enemata do nothing but exhaust the patient stimulate reverse peristalsis and increase distention and the rectal tube does nothing but cause piles. I have never seen it do anything else.

While all of us here know now and have known, of course, that this distention is

due to swallowed air, I can assure you that there are many people in this country who treat distention who do not yet know this, and who hold the older views that I have already hinted. I think it is very timely and very wise that these subjects be discussed and discussed more widely outside of the halls where this Association meets.

I was very much interested in Doctor Singleton's mention of the method of preventing distention by the use of the tube introduced before anesthesia. In our own laboratory Doctor Moyer has carried on experimental work, and has shown that particularly in the excitement stage and in the presurgical stage of cyclopropane anesthesia, and to a lesser extent ether, enormous amounts of air may be taken in. For example, a dog weighing from 10 to 15 Kg may take in, and has taken in under these circumstances, by swallowing, just at this stage and not in the deeper anesthesia as high as 1500 cc of air in three minutes. Associated with this intake, of course, there is always a fall in blood pressure of ten to 35 points and rapid respiration, and, of course, if carried on it may come to the point where death of the animal will ensue. I had not appreciated how much air can be taken in just at this time namely, during the early part of the operation. With the tube in the stomach as Doctor Singleton mentioned, the air is drawn back very quickly and this difficulty is obviated.

Both essayists have mentioned again briefly, something we all know and something that deserves a great deal of further study, and that is the diminution in the vital capacity in the available air the residual air associated not only with the operation. We also know that distention further inhibits the action of the diaphragm, and we all, of course, know that this minimizing of the action of the diaphragm renders that patient quite susceptible to atelectasis which is the commonest of all pulmonary complications. It has been shown many times that anoxia is always associated with the diminution of the vital capacity and anoxia plus the proneness to atelectasis should, I think be emphasized again as a very disturbing side light on distention.

There is one phrase that Doctor Singleton used that I think perhaps may be a little misleading 'fluid gained'. I think it would be better for Doctor Singleton to say fluid retained. Fluid gained rather implies this is a gain in the total weight of the patient. We know that is not true. The amount that is retained is important. Of course, but it is never enough to supply the fluid needs of the body.

Your measurements of course show that 4 Gm is an average loss of salt per day, which is about a liter of gastric juice. In our clinic—Doctor Maddock presented this to you two years ago—we have found a very satisfactory way of taking care of the salt requirements by replacing it by the so-called volume-for-volume rule. It is lost as hypertonic, and if one replaces that amount with the normal saline the salt needs of the patient will be cared for without giving an additional dangerous amount.

In conclusion I would like to urge this society to take the same firm stand against the use of enemata as we have for long years taken against the use of cathartics in cases of distention.

DR PHILEMON E TRUESDALE (Fall River, Mass.) I was very glad to hear Doctor Singleton refer to dilatation of the stomach and its consequences, because I think it is important in case one cannot decompress the stomach by an ordinary small stomach tube. As the stomach increases in size from gases, it continues to enlarge toward the left side and raise the diaphragm. As it increases in dimension, and as the pressure in the stomach increases, there is an angulation at the lower end of the esophagus at the cardiac sphincter, and as the stomach continues to dilate the diaphragm rises and when the pressure in the stomach has reached a point that is greater than it is in the left pleural cavity, the diaphragm continues to rise until it is in position of eventration. In this position of eventration it displaces the heart and it displaces the entire mediastinum causing pressure on the right lung, and then, as the pressure increases, the right lung is encroached upon further, and there is an anoxemia.

Now the Miller-Abbott tube under such circumstances is not adequate because it does not drain the stomach, but a small stomach tube of more rigidity than the Miller-Abbott tube will pass through the cardiac sphincter.

I just wish to call your attention to this point in case of disappointment in using the Miller-Abbott tube at that time, that the use of a more rigid rubber tube, the stomach tube, will pass into the stomach, although the displacement of the thoracic organs has developed to a considerable degree.

DR WALTER G MADDOCK (Ann Arbor, Mich) One of the points I would like to know more about is the mechanics of swallowed air Doctor Singleton has mentioned one of the possibilities, in the fact of air getting down into the stomach during anesthesia It has always seemed to me that I have never seen patients with intestinal obstruction and a lot of distention, doing a great deal of air swallowing

I have been interested in the problem, and I recall one case vividly, of a child of four who had peritonitis from a ruptured Meckel's diverticulum We had a plain film of abdomen, and it showed a tremendous pneumoperitoneum, the liver and the spleen clearly outlined, and the intestines outlined in the center of the abdomen We put a trocar through the abdominal wall and let the gas whistle out, and it did, under considerable pressure The patient was operated upon about 40 minutes later, being unconscious in the meantime The pulse was about 160 per minute, respiration 60 By the time that patient got to the operating room the distention—that is, the pneumoperitoneum—was up just as high as it was before we put the trocar into the abdomen

I am sure there is some mechanism by which that gas gets down into the gastrointestinal tract, and in that case into the peritoneal cavity that is not actually swallowing But it is true that is largely atmospheric air

I have made one experiment in trying to determine how gas gets down I do know that on respiration the esophagus opens up The bronchoscopist will tell us the same thing And the air goes right down the esophagus In my efforts to see whether it would pass into the stomach in dogs I failed to find that a definite fact I thought it occurred in a couple of cases but the evidence was not conclusive I think it is an interesting point to keep in mind that while we are using the term 'swallowed air' we still have got a lot to account for in knowing more about the mechanism of the act of swallowing

DR ALBERT O SINGLETON (closing) Doctor Collier is a young man, but he did mention the fact that he remembered when a great many things were done to prevent gastric distention I know quite well that I spent much more time with the rectal tube when I was a hospital resident intern than I did with the stethoscope in trying to get rid of gas in postoperative patients

Ileus without distention does not seriously hurt a patient The bowel may not have peristalsis for a very long time still if there is little air or gas in it that patient does not become ill

Doctor Gatch told us many ways in which this distention affect the patients If one gets a patient before distention occurs it does not matter what the pathology is one can prevent the distention from occurring

We are convinced after very long and careful study of these patients that no patient gets distention so long as the gastric suction tube is working This may be five six, or seven days He will be just as flat when you see him five days after operation as he was at the time of operation The time for gastric suction is before distention occurs The place for intubation of the intestine is after the distention occurs

Generally speaking most patients reach the surgeon before distention becomes marked even in peritonitis and appendicitis If they are operable they are not very badly distended Following the operation they should not become distended at all If you keep the gastric suction working until peristalsis is restored even though it be a week, the patient will be just as flat and as well off when you get ready to take the suction away The amount of gas that may accumulate in the intestine in a short time is amazing Occasionally we remove the suction too soon or the suction tube gets stopped-up within three hours the patient will be ballooned up and trying to vomit

So, by preventing gaseous distention one goes far to make surgery safe, not only abdominal surgery but thoracic surgery is well If one keeps the gas out of the alimentary tract for three or four days after the pneumonectomy the patient aerates himself much better and does not become so ill So the possibilities of this procedure simply keeping the air out of the intestine makes abdominal surgery much safer than it has ever been before

SMALL INTESTINE OBSTRUCTION A FIVE-YEAR STUDY

R J NOER, M D , AND CHARLES G JOHNSTON, M D

DETROIT, MICH

FROM THE DEPARTMENT OF SURGERY, WAYNE UNIVERSITY COLLEGE OF MEDICINE AND THE DETROIT RECEIVING HOSPITAL

SUFFICIENT time has elapsed since we began a rather extensive use of intestinal suction drainage to permit an analysis of our results over a five-year period. This series includes all cases of small intestinal distention or obstruction treated on the Wayne University Surgical Service at the Detroit Receiving Hospital between January 1, 1937 and January 1, 1942. It is to be emphasized that we have included all cases with sufficient distention to require treatment, whether or not the distention was the primary condition for which they were admitted. There were 332 such cases, this number representing approximately half the total number admitted to the hospital during that period.

For simplicity of classification we have chosen to use that described by Crowley and Johnston (Fig 1) since it considers the three important factors in all cases of ileus: patency of the lumen, peristaltic power, and circulatory status. Space limitations do not permit detailed consideration, but the results will be briefly listed according to this classification.

OCCLUDED ACTIVE ILEUS—112 CASES

These are cases in which the primary factor is occlusion of the lumen of the intestine, commonly referred to as "mechanical obstruction." One hundred and twelve or about two-thirds of our 332 cases fell in this group. Adhesions were the most common cause, accounting for 94 of the 112 cases of occlusion. (The figure given includes a number of cases of strangulated obstruction more fully described elsewhere.) Twenty-one of these 112 cases of occluded active ileus died, a mortality of 18.7 per cent for this group, this includes all deaths, whether or not directly attributable to the obstruction.

PATENT INACTIVE ILEUS—135 CASES

Loss of intestinal propulsive power is the primary factor in this group, it is the one commonly referred to as "adynamic ileus" or "paralytic ileus." Minor degrees of distention have not been included, this report considering only cases in which the accumulation of gas was sufficient to require active treatment for relief.

Postoperative ileus (47 cases) and that associated with peritonitis (54 cases) comprise more than two-thirds of this group. Twelve cases followed trauma and 22 were the result of various other conditions, among them pneumonia, uremia, liver abscess, and pancreatitis. Twenty-five of the cases in this group died, a mortality of 18.5 per cent for the entire group, this includes all deaths, whether or not directly attributable to the distention.

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ILEUS-TYPE INDETERMINATE OR MIXED—29 CASES

There will always be certain cases in which it is nearly impossible to determine whether luminal occlusion or inactivity of peristalsis is the primary factor. Certain other cases, particularly those with inflammation producing both reflex intestinal inhibition and occlusive adhesions, can only be listed as belonging to both groups. To avoid duplication these are listed in a separate category of 'Ileus-type Indeterminate or Mixed', there were 29 such cases.

Five cases were undiagnosed, presenting marked distention when first seen, they were decompressed by suction drainage and thus relieved of their symptoms. They were not operated upon, roentgen ray localization studies failed to reveal obstruction and they did not redistend subsequent to removal of the tube.

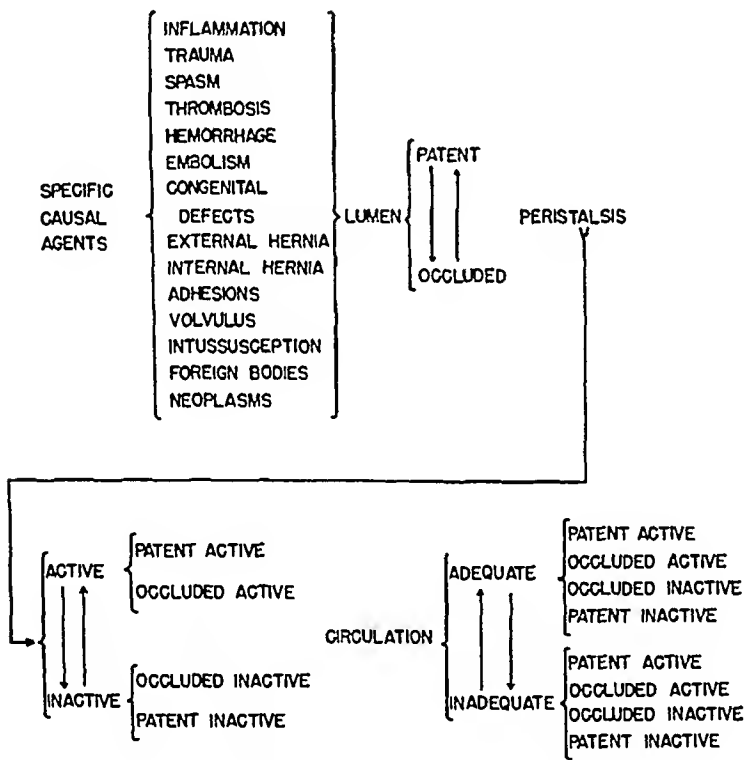


FIG. 1—Scheme for classification of small intestine ileus (Crowley)

Twenty-four cases had both adhesions and inflammation or malignancy and inflammation. This group includes most of the peritonitis cases, hence the high mortality of 12, or 41.7 per cent, of the 29 cases in this group.

INTERFERENCE WITH THE MESENTERIC BLOOD SUPPLY—81 CASES

The mesenteric circulation can be impaired either by strangulation in external herniae or by pressure from some agent within the abdomen, in either circumstance immediate operation is imperative. Because of differences in ease of diagnosis, these two groups are separated for study.

(I) *Internal Strangulation*—25 Cases—Seven of these were due to

adhesive bands, 12 to volvulus, four to internal herniae and one to intussusception. There was one case of mesenteric thrombosis. Operation was deferred in three cases and not carried out in three others, in five of these, diagnosis was in error or delayed, while the sixth was moribund on admission. Internal strangulation was thus correctly diagnosed preoperatively in 19 of the 25 cases. Ten of the 25 died, a mortality of 40 per cent for the group.

(II) *Strangulation in External Herniae—56 Cases*—Included here are only those cases of strangulated hernia which showed definite color changes of the herniated intestine, with or without petechial hemorrhages in the mesentery. These cases were not included in the study as originally planned, but have been added for the sake of completeness.

Among the 56 cases were 34 inguinal, 13 femoral, five ventral and four umbilical herniae. Four required resection of intestine, and three of these died. In all, eight cases died, a mortality of 14.3 per cent for the hernia group.

METHODS OF TREATMENT

Throughout the period covered by this report, our primary consideration has been the relief of distention, usually by some type of suction drainage (gastric 53 cases, duodenal 39 cases, intestinal 180 cases). Enterostomy was performed but five times, cecostomy twice. In most of these cases the procedure was a futile gesture and had little effect upon the outcome.

In occluded ileus, operation was carried out within the first 24 hours when mesenteric vascular interference was suspected or when the cases were seen early before marked distention had developed, all other cases were subjected to a period of preparatory decompression with concurrent restoration of lost fluid and electrolytes. Nonoccluded cases usually required only decompression, fluid and electrolytes, and treatment of the primary disease condition which caused the distention.

SUMMARY

(1) Three hundred and thirty-two cases treated for small intestine obstruction, with or without distention, have been studied and the results briefly summarized.

(2) Fifteen, or 4.5 per cent of the deaths, were directly attributable to the patients' obstruction. Distention, however, may well have been an important factor in many of the 43 other deaths.

(3) Therefore, we feel that the total number of deaths, from whatever cause (66), is the figure which should be considered. This makes the mortality 19.9 per cent for the entire group.

DISCUSSION —DR ALLEN O. WHIPPLE (New York) There are two points that I should like to bring out in connection with the last paper. Our clinic has been a very strong advocate of intestinal intubation and we now have some 510 cases that have been intubated. I am not going to go into the details of statistics but I want to bring out two points, or discuss two phases of this subject. One is the so-called paralytic or dynamic ileus. Doctor Lee, of our clinic, has recently published a study of a series of cases in which a paralytic ileus was very definitely associated with a low serum protein and a definite evidence of edema of the bowel. Many of the cases of peritonitis where there has been a marked loss of protein in the exudate in the peritoneum developed this type of peritonitis. Another group,

which was the result of overhydration and overenthusiasm in giving salt solution in the presence of a low serum protein developed this same type of edema of the bowel wall, causing a loss of function of the bowel

The other group of cases that I would like to speak of is that of right colonic resection. Intestinal intubation in that group of cases has produced an amazing lowering of mortality in our clinic

In some 39 where intestinal intubation has been used as a preoperative measure we have lost only one case. That is based upon a very definite and sound surgical principle, and that is that you remove tension from the suture line. I am not speaking of the right colon section with ileocolostomy. Whether that is an end-to-side or side-to-side anastomosis I do not think makes much difference but the keeping empty of the proximal loop of intestine that is sutured to the colon makes it possible for the initial sealing-off of the peritoneal suture line, the prevention of tissue necrosis due to distention, and insures a smooth postoperative course.

The combination of intestinal intubation, together with the preparation of the patient beforehand, bringing his metabolism to normal level before operation, and the use of one of the sulfonamide compounds sulfanilamide or sulfadiazene by way of frosting the anastomotic line I believe will make a tremendous difference in the right-sided colectomies. In left-sided colectomies, the intubation is of relatively little use, and in those cases I am still firmly convinced that a preliminary cecostomy even in the absence of obstruction, is a very important safety factor but all of the measures that have been spoken of are really based upon the removal of tissue tension from the suture line and maintaining the blood supply to the intestine.

It seems to me that the intestinal intubation has introduced a new safety factor in abdominal surgery which cannot be overestimated.

DR R. J. NOER (closing). In regard to Doctor Gatch's statement about the internal strangulations and the delay in operation perhaps I did not make myself entirely clear on what we meant by immediate operation. Those which were listed in the tables as "immediate operation" were performed within the first 24 hours. Most of them had at least a few hours' delay for restoration of their fluid and chemical balance. Thirty-one cases were operated upon within the first 24 hours and 25 had later operations.

We are not willing to bring ourselves to the point which Doctor Gatch suggests that even in the presence of internal strangulation these patients can be allowed to wall-off as does an appendiceal abscess. However we did have an interesting patient received from another service rather late in the course of her disease who had a large mass and evidence of intestinal obstruction for many days. Her abscess was drained and the patient subsequently died of pneumonia. At autopsy we found that about two feet of intestine had sloughed off and a fairly good anastomosis had been established. She was not treated that way by election, but it is mentioned as an indication that what Doctor Gatch says does occur.

With regard to Doctor Truesdale's statement about the difficulty in passing the Miller-Abbott tube into a dilated stomach, I might say that for several years we have almost never used the standard commercial Miller-Abbott tube, partly because of its greater degree of flexibility. We make up our own balloon-tipped tubes with a No. 16 or No. 18 Jutte tube. This is stiffer and much easier to manipulate and we believe just as efficient in the stomach or duodenum as the standard stomach or duodenal tubes.

We would certainly agree with Doctor Singleton on the use of the stomach tube in prophylaxis. We find, as I mentioned, with cases of peritonitis that with a tube in the stomach a fair number of these patients never become distended, and the intestinal tube is therefore not required for treatment.

VITAMIN DEFICIENCY AS A FACTOR IN THE ETIOLOGY OF SURGICAL DISEASES OF THE DIGESTIVE SYSTEM¹

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DESPITE the tendency of vitamins to become a fad and with the opportunity they provide for commercial exploitation, definitely known facts about them appear to merit attention. The reality of certain vitamins, and their influence on certain diseases, seems well proven. Inadequacy of vitamins B, C and D as causative factors in beriberi, scurvy and rickets, respectively, is recognized. On the other hand, it is felt that other pathologic conditions may be due to vitamin deficiency, although it is difficult to prove which vitamin is involved, or it may be that the lack of more than one vitamin is responsible.

Surgery is concerned but very little with the diseases mentioned above, and it is found that most diseases in which avitaminosis plays a part rarely require surgical treatment. However, it is important for the surgeon to consider carefully vitamin deficiencies as part of the preoperative and postoperative care of patients. The direct, immediate causes of the lesions under discussion, ulcer of the stomach and duodenum, gallbladder disease and appendicitis, sometimes are understood and often are not. It is with the remote, underlying, or predisposing causes that we are concerned in this paper. Such causes also might be classed as preventable, which direct causes are not.

Interest was aroused in this subject 35 years ago when the scarcity of these diseases was observed among the Negro patients in the Grady (municipal) Hospital, Atlanta. Appendicitis was rare among Negroes as compared with white patients, while the presence of a stomach ulcer or case of cholecystitis on the Negro wards created a sensation and all the staff wished to see it. The absence of these lesions in the colored population was explained on the ground of "racial peculiarity." The neurogenic origin of ulcer, suggested years later by Cushing, of course, was not thought of.

The remarkable paper of the British surgeon, McCarrison,¹ 21 years ago, gave a different idea. He wrote that during nine years' sojourn in a remote part of India he performed 400 surgical operations annually among the natives, and during this time he did not see a single case of gastric or duodenal ulcer, appendicitis or ulcerative colitis. Gallbladder disease was not mentioned, and ulcerative colitis is removed from the present discussion because the sulfonamides have almost eliminated this lesion as a surgical entity. At the same time, ulcerative colitis has been as uncommon in Negroes as gastric ulcer.

McCarrison decided that the absence of these diseases among the East Indians was due mainly to the character of the food which they ate. Their food came from the area in which they lived—milk, eggs, grains, fruits and vegetables. They indulged in very little meat, and the amount of sugar consumed in a community of 30,000 people in a year was not as much as used in one of our large hotels in one day. McCarrison believed that the fresh, natural foods

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

of the natives abounded in vitamins, and that the presence of vitamins was a factor in the prevention of these diseases. Specific vitamins were not designated, their identity was not so well recognized as today. That it was not necessary to ship the foods any considerable distance, and that they were eaten soon after being harvested, made preserving them by canning and other means unnecessary thus maintaining their maximum vitamin strength.

McCarrison had evidence that racial peculiarity plays but a small part in the etiology of certain diseases. He watched the health of a large group of natives who had been under his care and who were compelled to move to another district where their former foods were not available. Immediately many of these people developed sicknesses which did not affect them while partaking of their accustomed nutriment. McCarrison at this time further proved his contention as to the results of faulty foods in experiments upon wild monkeys made to subsist upon unnatural, artificially prepared diet.

Another proof of the small part played by racial peculiarity in the cause of disease is shown by Garber,² in his study of the Eskimos. His paper also indicates that vitamins are factors in the prophylaxis of the diseases under consideration. He states that "such maladies as appendicitis, stomach and bowel disorders, cancer, dental decay and many other diseases in the category of the white man's bodily ailments are unknown to the Eskimo. But as soon as he abandons his own diet of fish and meat, even in part, and begins to eat the white man's food, all these ailments appear." Upon what flesh does the Eskimo feed that he does not have the stomach ache? It is well to say "flesh" because he subsists entirely upon flesh—and fish, no bread, no fruit, no vegetables. Such food must be rich in vitamins since this is the only opportunity to obtain them. Thomas³ tells us that fish subsist largely upon marine vegetation, and reminds us that all "flesh is grass." Thus meat and fish come from plant life, the chief source of vitamins.

The question is often asked "Since Reginald Fitz called the attention of the profession to appendicitis only in 1886, how long before that time was the disease supposed to exist?" While our predecessors in medicine of 200 years ago did not possess the facilities for diagnosis which it is our good fortune to have, nevertheless they were intelligent men, and good observers, and if such a disease as appendicitis had been at all prevalent they would have recognized it and would have written about it. No doubt there were some cases, generally called peritonitis, or something similar, but no considerable number of such cases is recorded. The proposition is advanced, therefore, that appendicitis is mainly a disease of the nineteenth and twentieth centuries.

Gastric and duodenal ulcers and cholecystitis may be grouped with appendicitis in the discussion. It is impossible to explain satisfactorily just why these lesions have appeared in such vast numbers only so recently. The rôle played by avitaminosis is suggested as a partial answer to the problem. The exigencies and complexities of modern life have prevented man from eating only the foods raised in the area where he lives. It now seems essential to preserve large quantities of food and transport them great distances when the customs of the modern table require many of them to be overprepared before

they are consumed. Canning is the principal means of preservation, and while this method may not lessen other nutritive values, there is evidence that canning destroys or impairs vitamin content. The canning of food came into existence in 1810, and was invented by the Frenchman, Nicholas Appert, acting under the instigation of Napoleon Bonaparte. Before this time certain foods had been preserved by drying, pickling and smoking, but were not at all in common use. Napoleon, asserting that an army travels on its stomach, desired to give his soldiers foods retaining as nearly as possible their natural condition by keeping fruits, vegetables, meats, broths and milk in a moist or liquid state. Thus began the era of the home and commercial preservation of foods in cans and other air-tight containers, which, while apparently unavoidable and necessary, may have had something to do with bringing about the era of vitamin deficiency and the introduction of new ailments for the human race.

Experimental evidence is wanting as to the relation between vitamin deficiency and gallbladder disease and appendicitis, but Smith and McConkey⁴ and others have presented graphic demonstration of the relation of vitamins and "peptic"* ulcers in guinea-pigs. In a previous paper⁵ these authors had shown the connection between lack of vitamins and tuberculous ulceration of the intestine. Routine necropsies on 1000 guinea-pigs fed on stock diet did not reveal a single peptic ulcer. Of 75 pigs fed on diets lacking vitamin C, 26 per cent developed peptic ulcers which were similar in location and in gross and microscopic appearance to those observed in man. Diets deficient in vitamins A, B and D did not cause peptic ulcers if the supply of vitamin C was adequate. Mechanical injury to the mucosa of the duodenum in guinea-pigs fed on an adequate diet was followed by rapid and complete healing, while similar injury to guinea-pigs fed on a diet deficient in vitamin C resulted in the formation of peptic ulcers. Smith and McConkey concluded that peptic ulcer in the guinea-pig apparently is caused by a partial but prolonged deficiency of vitamin C.

The incidence of surgical diseases of the digestive system has increased among the Negroes of the South since the first observation was made 35 years ago, due it is believed, as will be shown, to a changing diet. The difference in the number of cases in the two races, based on the percentage of population, is still marked enough to bear out the claims of the present discussion. Nine general hospitals supply the metropolitan area of Atlanta, embracing a population of 533,000—381,000 white, and 152,000 colored. There are seven hospitals for white patients, and two for Negroes. The vast majority of the patients in this district patronize these institutions, many patients come from other parts of the state and country, while a considerable number of patients go to hospitals outside the territory. During the past five years (1937–1941), among white patients admitted there were 1343 cases of ulcer of the stomach and duodenum, 2940 cases of gallbladder disease, and 16,372 cases of all types of appendicitis. During the same period, among colored patients admitted there were 130 cases of ulcer, 98 cases of gallbladder disease, and 974

* Used for brevity, "gastric and duodenal ulcers" is preferred

cases of appendicitis. These figures, which are approximately correct, show that during the past five years ulcer was eight times as common in white patients as in Negroes, gallbladder disease was 15 times as common, and appendicitis eight times as common. Inquiry reveals the fact that the relative frequency of these diseases in the two races in other Southern cities is about the same as that reported from Atlanta.

The question has been asked whether the Negro patients receive as thorough study as the white patients. The Negro Division of the Grady Hospital is operated by the Medical School of Emory University, so that these patients are assured diagnostic and therapeutic care on par with that of white people. Again, inasmuch as an equal number of white and colored patients, 50,000 of each, were treated in the hospital during the five-year period, 1937-1941, and since the colored population of the Atlanta area is less than one-third that of the whites, it is probable that more than 90 per cent of the Negroes afflicted with the lesions under discussion were treated in the Grady Hospital. A small per cent were unrecorded, or were treated in a private hospital for colored patients.

The food of the Southern Negro compares in a measure with that of McCaullison's East Indians, and probably would be exactly duplicated if possible. The Negro's first choice in diet is fresh green vegetables, turnip greens, collards and cabbage, and a mixed juice made from them, called "pot likker." They enjoy other vegetables like cow peas, string beans and potatoes, and eat various cereals. Their favorite bread is corn bread, made from water-ground meal when it can be obtained. They will eat fresh fish every day if they can get it, but do not consume a great amount of meat, except the cheaper kinds of bacon, and are not especially fond of sugar and sweets. Pork chops are highly esteemed but are not generally included in the menu on account of the expense. The same reason applies to chicken despite the Negro's traditional affection for this fowl. Coffee and tea do not appeal to their appetites, but they relish lemonade, even for breakfast. High cost precludes liberal use of milk and eggs. In contrast with the more expensive, over-prepared food of most of the white inhabitants, according to our knowledge of the subject, the chosen nutriment of the Negro, while cheap, is rich in vitamins.

Close inquiry reveals the fact that most of the colored victims of the diseases under discussion have strayed from the foods listed above, and either from choice or necessity have indulged in the fare of modern civilization. Some of these patients lived in the homes of white people where they could not obtain a sufficient amount of the nutriment which agrees with them so well, or their occupation forced them to dine at lunch-counters where the can-opener is used so freely. Negroes do not eat canned foods, and it is most unusual to find such an article in their homes. As the members of this race take on more and more the dietary of the day, however, alimentary diseases increase among them.

The loss of vitamins by canning varies with the kind and condition of the food used, and the method of canning. Improved methods are in vogue today which seek to preserve vitamins and other nutritional qualities by the elimination of all air from the cans. The analysis of raw, cooked and canned samples

from various sources, given by Pett and Cantor,⁶ show the stability of vitamins under canning as follows

Vitamin A is fairly stable to heat in the absence of air, and loses from 10 to 50 per cent vitamin content from canning, whether in the home or factory

Vitamin B₁ is appreciably destroyed in all cooking and canning. Acid products preserve it best, the loss of being 5 to 15 per cent, but in alkaline products 80 per cent may be lost

Vitamin B₂ complex is more stable to heat. Riboflavin and nicotinic acid are destroyed to the extent of 5 to 20 per cent

Vitamin C is the least stable of all vitamins, but owing to the occurrence of precursors or combined forms it is stable to canning in some foods, in other cases it is completely destroyed

Vitamin D is fairly stable in milk, it is not important in most other foods

These authors conclude that since canned foods must be cooked again in the home, further losses in vitamin content will be noted. This fact tends to bring the value of canned foods even lower than foods which require only one cooking. Therefore, canned foods may sometimes be justified mainly on grounds of convenience and price rather than for their food value

While vitamin deficiency is only suggested as one of the causative factors in the production of these lesions, further experimental work may result in more definite proof. Infection is one of the principal etiologic agents in cholecystitis and appendicitis, and it has been shown in the laboratory that lack of Vitamins A and B complex lowers resistance to infection from 50 to 75 per cent.⁷ Study of the cause and prevention of disease is equally as important as its diagnosis and treatment

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DISCUSSION—DR J. SHELTON HORSLEY (Richmond, Va.) This paper of Doctor Boland's is very interesting and thought-provoking. Those of us who were born and raised—I suppose I should say born and reared—in the South along with the Negroes, have evidently noted the change in the incidence of diseases, certainly during the last 25 or 30 years. The effect of vitamins on the Negroes and on the Whites is, of course, rather marked. The "pot liquor" that Dr. Boland spoke so eloquently about is probably one great source of vitamins. It has been made nationally famous by some of our Southern senators who use it in "dunking" but whether used that way or not, it does contain among other vitamins, considerable vitamin K, because as you know, vitamin K

comes from alfalfa, among other things. It seems to be not too much of an assumption to think it comes from that too. Vitamin K which, as you know, has almost transformed the surgery of jaundice, is extremely important and is synthetically prepared.

There is a very interesting correlation between the vitamins and the repair of wounds. It is common knowledge that ordinary wounds on patients who have some vitamin deficiency repair much more rapidly when this deficiency is supplied.

In regard to cancer, vitamins are recently becoming very interesting, especially vitamin H which has recently been offered and now prepared in crystalline form. Two years ago this was found to be one of the stimulating elements of growth and it was found in rapidly growing cancers. It may in a way now explain the cause of rapidly growing sarcomata in which there is a streptococcic infection. Vitamin H or biosin is found very abundantly in rapidly growing malignant tumors. It is also found abundantly in embryos and in young children.

The streptococcus also demands a large amount of biosin so that when a wound is infected with streptococci it may consume so much of the biosin that the malignant cells cannot live. That seems to be probably the most logical explanation of those cases in which cure has followed streptococcic infection or in those cases in which Coley's fluid has been followed by cure. While only a few there are undoubtedly some.

About six years ago a Japanese investigator found one of the benzene rings through the neozobenzene I believe called butter-yellow. It has no connection with butter. It is just called butter-yellow because it resembles it in color. It is a very remarkable karyogenic preparation. If that is fed to rats that are on a low vitamin diet of polished rice, carcinoma of the liver develops in about 90 per cent of the rats. Now, if the rats are given a fairly good vitamin diet, the carcinoma incidence drops to about ten. But if on the other hand they are given biosin, the carcinogenic substance breaks through this resistance and goes up to 90 again.

There is a preparation of egg white called abidon that seems to counteract the effect of biosin to some extent. While that looks like suggestively a remedy for cancer clinically, does not work out.

Sydenstricker of Augusta, Ga., did some experiments on this, giving large quantities of it and produced symptoms quite like pellagra, avitaminosis. However, there is a possibility that something may arise through this. There are two different substances, one antagonistic to the other. Egg white abidon, of course, is in egg-white or albumin and can be extracted.

DR. FRED B. LUND (Boston, Mass.) I was delighted to hear Doctor Boland call attention again to the importance of vitamins among patients who have surgical diseases. As some of you know, I have studied some of the vitamins, particularly vitamin C.

In our thinking about these vitamins, we have to be quite careful about drawing definite conclusions as to cause and effect. As recently as seven years ago, some very excellent observers stated that lack of vitamin C was a contributory cause of secondary anemia. Two years ago the same observers restudied the problem a little more carefully and came to the conclusion that they had been wrong the first time and that what had occurred was that the patients who came into the hospital with dietary secondary anemia were suffering from two separate diseases: that the same diet that was deficient in iron was also deficient in vitamin C, but the vitamin C deficiency had nothing to do with the anemia.

Gastroduodenal ulcer in the human has not, so far as I know, been shown to be caused by lack of vitamin C. I have some data, which are as yet unpublished, showing that 90 per cent of the patients with gastroduodenal ulcer, as seen at the Boston City Hospital, have less than saturated levels of vitamin C in the blood, but just a few patients come in with ruptured gastric ulcer, with obstructive gastric ulcer, bleeding gastric ulcer, who have been taking sufficient orange juice or other sources of vitamin C, and have perfectly normal reserves.

The situation in regard to the low vitamin C I think is a matter of choice of food and the fact that the population as a whole and many of the doctors have not caught on to the fact that if you push the milk and cream up very high in the diet and do not make a special effort to call their attention to the things removed from the diet, the patients themselves will be apt to remove too much of the vitamin C foods.

APPENDICITIS IN INFANTS AND CHILDREN

A FIFTEEN-YEAR STUDY *

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APPENDICITIS occurring in childhood is the most common lesion of the abdomen requiring surgical intervention. The symptoms of the disease are easily recognized where the patient is seen early and an early diagnosis made by process of elimination. However, gangrene and perforation, which occurs earlier in the course of the disease in infants and children, alter the subjective and objective findings and it is frequently difficult to evaluate the clinical picture. The adult is conscious of the discomfort associated with appendicitis and can describe his symptoms. The condition in the young child, however, may go unrecognized and not be appreciated because the symptoms are thought to be the result of a disease other than that involving the appendix.

This study of 1,653 case histories has served to emphasize certain facts. Chart I indicates that there is a progressive increase in the incidence of appendicitis in children up to ten years of age. The repeated administration of some type of cathartic is the rule rather than the exception in the group under consideration. Delay in seeking proper medical attention for many of these patients frequently after several days of illness has been a factor in the development of a well advanced infection at the time of admission, and has tended to complicate the surgical management. Pain is recorded as the outstanding subjective symptom accompanied by nausea and vomiting, although the latter may not be present. Fever is found in the majority of cases. The history, as given either by the parent or child, reveals that the onset of pain was sudden and more or less general around the umbilicus, localizing later, usually in the right lower quadrant. Frequently, the objective findings relating to posture, namely, flexion of one or both thighs on the abdomen together with localized tenderness, rigidity or distention, served as an aid in making the diagnosis. In the group seen early in the course of the disease, the characteristic subjective and objective symptoms indicated immediate surgical intervention. Early operation is necessary in the case of the infant or young child. Procrastination leads to a serious condition which jeopardizes the child's chance for recovery, in spite of the best surgical management.

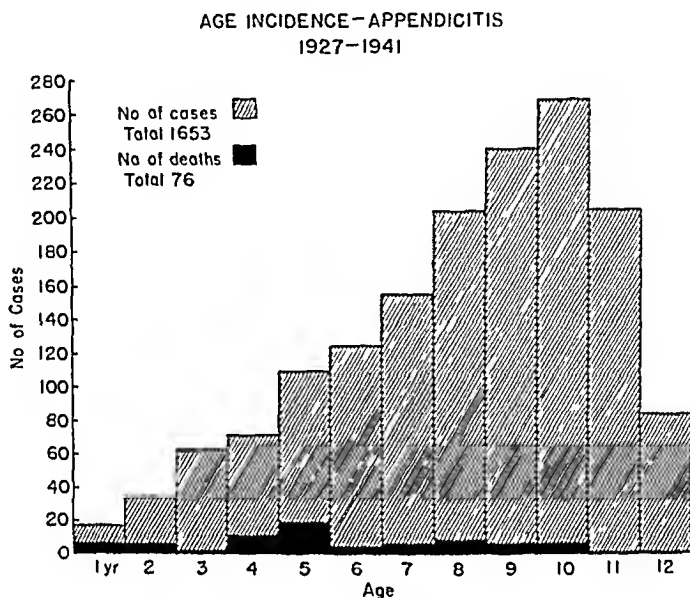
The important problem which confronts the surgeon is the decision regarding the advisability of an immediate operation on the child ill for several days with dissemination of infection throughout a considerable portion of the peritoneal cavity. Individual consideration should be given each patient and certainly no rule can be formulated which sets up an arbitrary type of surgical

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

management There is, however, general agreement that the patient ill for several days, dehydrated and with abdominal distention, requires a period of conservative treatment to improve the general condition preparatory to surgery

CLASSIFICATION AND DISCUSSION

This study of appendicitis occurring in infants and children under age 12 includes a review of many patients in the charity class, often undernourished and with low resistance to infection We believe this fact should be considered in evaluating the results of treatment



All cases of acute appendicitis have been classified in the following groups (1) Acute unruptured appendicitis (2) Local peritonitis (3) Diffuse peritonitis (4) Abscess

(1) *Acute Unruptured Appendicitis*—The acute unruptured appendicitis group included 742 patients operated upon with three deaths, or a mortality rate of 0.44 per cent. The causes of death were (1) Pneumonia on the fifth day, (2) intestinal obstruction on the sixth day, and (3) patient died suddenly at the conclusion of the operation, the cause of death was not determined. From the above experience, it is apparent that early diagnosis and immediate operation will give good results. This paper is not particularly concerned with this group of patients, because the morbidity and mortality is minimal.

(2) *Local Peritonitis*—This group includes the children admitted after an illness of several days' duration with clinical evidence of appendicitis with perforation and local peritonitis. Often considered poor risks at the time of admission, practically all of these patients can be successfully prepared in a few hours by reestablishing hydration. At operation, drainage may be established, and the ruptured gangrenous appendix removed, if this procedure does not unduly increase the time factor or present the possibility of increased contamination of the peritoneal cavity. Chemotherapy and intestinal siphonage are a

valuable adjunct in the management of these cases. There were 183 patients in this group who were operated upon in the 15-year period.

(3) *Diffuse Peritonitis*—We are particularly concerned with the patients in the third group, which includes children in the underprivileged class admitted to the Surgical Service late in the course of the disease. The picture is often that of a well developed paralytic ileus associated with a high temperature and a rapid, weak pulse. Efforts to prepare these patients for operation have frequently produced little response, and it has been impossible even to attempt simple drainage. Many of these children have rapidly succumbed to the overwhelming toxemia a few hours after admission. Bacteriologic studies from peritoneal aspirations in many of these patients have revealed the presence of mixed infection. With the introduction of chemotherapy, some of these patients have responded satisfactorily and surgery has offered a better prognosis. Duodenal suction or the use of intestinal siphonage has also materially influenced the prognosis and has proved a valuable adjunct in preparing these seriously ill patients for operation. There can be no question but that these methods of intestinal decompression and drainage have contributed in lowering mortality in a group of seriously ill patients. There were 94 patients included in this group.

(4) *Abscess*—The fourth group of patients, those with localized collections of exudate, are not as serious a problem. The small abscess may or may not be drained at the time, according to the discretion of the surgeon. Short periods of preparation may often be indicated before operation. Our experience has indicated that many small abscesses will rapidly resolve. The large abscesses often are poorly handled by the patient and always present the possibility of rupture and spread of infection of clean areas of the peritoneal cavity. Therefore, in our opinion, relatively early drainage is the procedure of choice. If the appendix is not removed at operation, or in the case of the small abscess allowed to resolve, the parents are instructed to return the child for appendectomy within a period of two months from the time of discharge from the hospital. There were 292 patients diagnosed as having an appendiceal abscess and all were operated upon, although in many instances the surgical procedure was limited to drainage alone. A number of patients not listed here recovered without operation and were discharged to return later for appendectomy. They were then included in the chronic or recurrent group.

PREOPERATIVE MANAGEMENT

The preparation for operation of the child seriously ill as the result of appendicitis with perforation is particularly important. The establishment of physiologic rest of the intestinal tract is indicated as an aid in the prevention of a further spread of infection. This is accomplished by withholding all fluids by mouth, suction drainage, heat to the abdomen and sedation. The patient's fluid balance is reestablished by the administration of saline and glucose solutions, either by multiple infusions or by the continuous drip method. Supplementing intravenous saline and glucose, patients may be given whole blood

or plasma as indicated. When avitaminosis is present in young children with serious peritoneal infection, vitamin therapy is indicated.

SURGICAL TREATMENT

The response to preoperative treatment will decide the time for surgical intervention. The extent of the surgical procedure in the case of the critically ill child with peritonitis must be limited and the decision made as to whether drainage alone is indicated or whether appendectomy can be safely performed. Nitrous oxide and oxygen with a minimum amount of ether has proved a satisfactory anesthetic.

Incisions—There has been some controversy regarding the type of incision and its relationship to the mortality, especially in the patients with local or diffuse peritonitis. The McBurney incision is preferred by many surgeons. In the case of adults this choice may be justified, but in infants and children it is of less importance, because of the diminished relative distance between the pararectus (Battle) and the McBurney incisions.

During the past five years, 100 patients with acute ruptured appendicitis, with either local or diffuse peritonitis, have been operated upon. In 78 patients, the pararectus incision was used and there were two deaths. In the remaining 22 patients, the McBurney incision was used with three deaths. Good surgical technique and gentle handling of tissues is of greater importance and the mortality is not influenced by the type of incision used in the infant or child.

Drainage—All accumulations of pus and abscess pockets are opened and evacuated by suction. A soft rubber tissue drain is inserted either into the pelvis or iliac fossa depending on the location of the abscess. Counterdrainage through a small incision in the flank is established as indicated. In closing the wound, the peritoneum is sutured to the point of drainage and a rubber tissue drain inserted beneath the fascia. The remainder of the wound layers are sutured about the drain. In a few instances simple closure of the peritoneum and packing of the remainder of the wound with vaselined gauze have been practiced.

POSTOPERATIVE TREATMENT

Continuation of the methods of preoperative management are indicated until the patient is sufficiently improved to allow removal of suction drainage and discontinuation of the various supportive measures. The immediate continuation of intestinal siphonage following operation has proved of particular benefit as a prophylactic measure as regards paralytic ileus. The application of heat to the abdomen is a routine practice in the patient with distention. Oral fluids are withheld until the temperature and pulse rate approach normal and distention is satisfactorily relieved. Oxygen is also administered to the patient with marked distention. Whole blood or plasma transfusions have proved a valuable postoperative aid in cases of extensive peritonitis.

CHEMOTHERAPY

The sulfonamide group of drugs are gradually assuming more importance in the treatment of patients with peritonitis or abscess formation following

appendiceal perforation To date the total number of children in this study with intraperitoneal infection following appendiceal perforation who received chemotherapy is not large, but the results have been so encouraging that the continued use of the sulfonamide drugs is strongly indicated Prior to the year 1939, sulfanilamide was given orally to a few patients Although no definite conclusions were possible, our opinion at that time was not favorable in regard to this type of therapy With the introduction of sulfapyridine and subsequently sulfathiazole, the results with patients receiving chemotherapy were encouraging, although not entirely convincing, since the number treated was still small

The accompanying table lists all patients treated with the sulfonamide drugs during the years 1939, 1940, and 1941, a total of 47 patients for the three-year period One death occurred in the series, an 18-months-old child under treatment for pulmonary tuberculosis at the time the appendiceal infection developed This patient succumbed on the twenty-fourth postoperative day from bronchopneumonia All other patients survived, and in most instances the convalescent period was uneventful All patients receiving the sulfonamide drugs in the three-year

THE EFFECT OF CHEMOTHERAPY ON THE MORTALITY RATE IN THE PERITONITIS AND ABSCESS GROUP
THREE YEAR PERIOD, 1939-1941

No of Cases	Chemotherapy	Deaths	Mortality Rate
47	Yes	1	2.1%
67	No	8	11.9%

CHART 2

period had perforation of the appendix with local or diffuse peritonitis or abscess Twenty-nine patients were included in the abscess group The one death occurring in the series gave a mortality rate of 2.1 per cent During the same years, 67 patients in the peritonitis and abscess group did not receive this type of therapy There were eight deaths or a mortality rate of 11.9 per cent

It should be pointed out that as experience with chemotherapy indicated a valuable adjunct in the management of the seriously ill patient with peritonitis or abscess, relatively more children received the benefit of this treatment In most instances they were the seriously ill patients, the type that would ordinarily show a higher mortality It is, therefore, more convincing evidence that chemotherapy was of benefit since the mortality rate was relatively low

At present it is our rule to give during the postoperative period sulfathiazole intravenously in the form of the sodium salt to all patients with peritonitis of any considerable extent In addition, during recent months a majority of these patients have received sulfathiazole powder intraperitoneally at the time of operation In many instances the drug was also placed in the wound layers during closure Many patients received intravenous chemotherapy before operation and individuals treated conservatively without operation were given the drug parenterally as early as possible

As soon as advisable during the postoperative course, oral administration was substituted and continued until the temperature approached normal, and other evidence of peritoneal infection was absent

We are aware of the argument against the use of sulfathiazole powder intra-

peritoneally or in wounds, namely, the tendency to cake and to act as a foreign body, thus producing added peritoneal and soft tissue reaction. To date, we have seen little evidence that caking of the drug influenced the duration of symptoms or acted in any way detrimental to the patient's chances for recovery. To the contrary, the small group of patients in which the drug was given intraperitoneally or in the wound, without exception, recovered without an excess amount of drainage or delay in wound healing, or a prolonged hospital stay. The amount of sulfathiazole powder placed in the peritoneal cavity has been limited to 2 or 3 Gm. in younger patients and has not exceeded 5 Gm. in older children. Whether small doses of the drug are of benefit may be a question. On the other hand, the small quantities used may account for the absence of irritative symptoms.

Local chemotherapy in the less severe infections or nonperforated cases has not been a part of the management, but probably would prove of benefit as a prophylactic measure against possible contamination of the peritoneum or wound. These drugs have often been employed orally or intravenously in the treatment of complications, particularly pneumonia or upper respiratory infections, with good results as regards ultimate recovery and lowered morbidity.

The amount of sulfathiazole given intravenously or orally is determined according to the weight of the child, a total of 1.25 gr. per pound in a 24-hour period in divided doses at four-hour intervals. The blood levels are usually maintained at 3-5 mg. per cent, although occasional temporary levels as high as 15 mg. per cent have been encountered, usually early in the course of treatment. Unfavorable symptoms attributable to the drug require smaller doses or entire cessation of this type of medication. This has not been necessary in any of our cases to date. Sulfadiazine has been given orally to a few patients, but, since our experience with this drug is so limited, no conclusions can be formulated at this time.

TABLE I
APPENDICITIS—INFANTS AND CHILDREN
1927-1941

Classification	Number	Deaths	Per Cent Mortality
Acute unruptured	742	3	0.44
Acute ruptured—local peritonitis	183	1	0.55
Acute ruptured—diffuse peritonitis	94	61*	64.9
Appendiceal abscess	292	11	3.6
Recurrent (chronic) appendicitis	342	0	0.0
Total	1653	76	4.2

* Includes 35 unoperated

MORTALITY

There were 183 patients, or 11 per cent of the total number studied, admitted with a diagnosis of ruptured appendicitis and local peritonitis. There was one death in this group, or a mortality rate of 0.55 per cent. Postmortem examination revealed an acute dilatation of the heart and gangrene of the small intestine due to an adhesive band.

In the group classified as acute ruptured appendicitis with diffuse peritonitis

there were 94 patients, or 5.7 per cent of the total group of patients studied. Of this group of patients, 61 died, giving a mortality rate of 64.9 per cent. On further analysis, we find that 35 of the 61 deaths occurred without any operation having been performed. The condition of these patients on admission was critical and attempts to prepare them for surgical intervention were unsuccessful. There were 26 deaths, or a mortality rate of 44.1 per cent, in the remaining 59 patients in this group operated upon. Analysis of the deaths in this group revealed that these patients died of toxemia secondary to overwhelming peritonitis.

In the group classified as appendiceal abscess, there were 292, or 17.6 per cent of the total patients studied. There were 11 deaths, or a mortality rate of 3.6 per cent, with analysis of the 11 deaths occurring in the appendiceal abscess group as follows: one—Convulsions (ether?). Six—Pneumonia. Two Subphrenic abscess. Two—Peritonitis.

The patients with chronic or recurrent appendicitis are listed as a matter of record. There were 342 in this group, with no deaths.

In the groups classified as acute unruptured appendicitis, ruptured with local or diffuse peritonitis, or abscess, there were 1,311 patients, with 76 deaths, or a mortality rate of 5.8 per cent. The mortality for all groups was 4.2 per cent.

SUMMARY

(1) This study represents a review of 1,653 cases of appendicitis in infants and children occurring in a 15-year period (1927-1941) under the care of five members of the Surgical Service, The Children's Hospital of Michigan.

(2) Patients with acute perforated appendicitis with local or diffuse peritonitis require special consideration in regard to preoperative treatment, the optimum time for surgical intervention, the extent of the operative procedure, and the postoperative management.

(3) Chemotherapy in a limited number of patients has proved of definite benefit as an adjunct to the usual routine treatment.

(4) The early diagnosis of acute appendicitis and early operation are the most important factors in lowering the mortality of this disease in infants and children.

DISCUSSION—DR WILLIAM E. LADD (Boston). I am sure that most of us agree with nearly all of the statements that Doctor Penberthy has made. We certainly are all agreed that catharsis is contraindicated in appendicitis. We also would be unanimous in the opinion that delay in consulting a physician and a consequent late diagnosis is the chief factor in raising the mortality in this condition. I think most of us who have had much experience with this disease in early life would agree that the younger the patient the more important is the factor of early operation. The problem of acute appendicitis is no problem at all providing it is recognized and an operation is performed prior to the time that peritonitis or other complications have developed. The time limit between the onset of symptoms of appendicitis and the development of complications is apt to be much shorter in early life than it is in the later years.

In a review of 848 cases of acute appendicitis, made three years ago, at the Boston Children's Hospital by one of my associates, there were 466 cases of acute appendicitis with two deaths—one due to hemophilia, which was not recognized until after operation.

This mortality of 42 of 1 per cent is practically identical with the mortality of 44 of 1 per cent just reported by Doctor Penberthy. Other writers report similar negligible mortality in acute appendicitis before complications had developed.

I agree with Doctor Penberthy that delayed operation in these young patients who have developed peritonitis is a hazardous practice. Doctor Ochsner, of Chicago, who was the original advocate of the delayed operation in cases of spreading peritonitis, pointed out over 40 years ago that this practice should not be used in children. Opposition to the delayed operation does not mean that adequate time should not be taken to overcome dehydration and put the patient in the best possible condition for operation. On the contrary, this much delay is very often desirable and of great importance. The indiscriminate policy of delaying operation in cases of spreading peritonitis on the theory that the peritonitis will become a localized abscess is courting disaster in childhood. There is, however, an occasional case in older children in which the peritonitis may become localized and the case changed from the group of bad risks to a group of much lesser risk. To bring about such happy results requires meticulous attention to details of care and the nicest kind of surgical judgment. It should not be attempted in the home by the pediatrician or the general practitioner.

In recent years the McBurney incision has been resurrected, and in my humble opinion rather undue importance has been attached to this incision as a factor in lowering the mortality. If the cecum and appendix ride high up under the liver, a situation not too infrequently found in early life, a McBurney incision is awkward and undesirable. Likewise if the appendix can be palpated low in the pelvis the McBurney incision is not suitable. On the other hand if the appendix is retrocecal and the cecum is in the iliac fossa the McBurney incision affords an ideal approach. I think the best incision is one made over the appendix so that the offending organ can be removed with a minimum of trauma.

Regarding intestinal drainage by the Miller-Abbott tube it is our belief that the Miller-Abbott procedure will seldom be required if the ordinary Wingensteen gastric suction is used as a routine procedure applied at the time of operation and continued as long as indicated.

The addition of chemotherapy to our therapeutic measures appears to be helpful. In a report from our hospital prior to the use of chemotherapy there were 373 cases of peritonitis of appendiceal origin including the worst cases with a mortality of 6 per cent. Since the adoption of chemotherapy we have had 75 cases in which this factor has been introduced. Sulfathiazole has been the drug most frequently used and has been given in sufficient quantities to maintain a blood level of about ten. In these 75 cases there have been three deaths, a mortality of 4 per cent. One death took place on the fourth postoperative day, and one on the eighth postoperative day, with pneumonia as the determining factor as the cause of death. The third death took place on the eighth postoperative day, with intestinal obstruction and sepsis as the important factors.

In any given series the main factor in mortality will always be somewhat dependent on the extent of the sepsis at the time of operation. This factor is bound to vary in different localities and in different hospitals in the same locality.

DR. FREDERICK A. COLLIER (Ann Arbor, Mich.) I have no business discussing this paper at all because my experience in the care of acute appendicitis in youngsters is so much smaller than that of Doctor Penberthy and Doctor Ladd that it is quite inconsequential. Doctor Penberthy asked me to discuss the paper, however, and I think he did so because he regards me as one of the etiologic factors in perhaps raising his mortality there.

In 1930 we reviewed our cases in the University Hospital (adult and children) very carefully and we found that in both adults and children the death rate occurred essentially in one group—that is, the patients who came in having had the disease all with a cathartic from three to five days. They presented the typical picture so familiar to all of us, of generalized spreading peritonitis. Before that time we had followed the principle of removing the appendix so that the source of infection could be stopped. We concluded after this study that anything we did would probably give us better results than we had been getting because our mortality was between 50 and 60 per cent. So we determined at that time to pursue the policy of delayed operation.

Here again our differences between the policy we have been carrying out and the one mentioned by Doctor Ladd are not factual but only in the phrase I think because

after all Doctor Ladd hydrates these dehydrated youngsters, restores their chemistry, puts in a tube, decompresses them, and that is the essence of the delayed operation as we have carried it out. Our mortality in adults and in children is less than it was before.

Doctor Ladd puts his finger exactly on the difficulty, because one talks about delayed operation, and the wrong person delays the operation. It is not the delayed operation. The thing that does harm is the delay between the time of disease and the time the surgeon sees the case. I entirely agree that every one of these patients should be in the hospital under a surgeon's care, and one may delay for an hour, one may delay for ten hours, one may delay for a week. It requires in my opinion, surgical judgment that I do not have, and that very few do have, to know exactly what is the safe time. As a matter of fact, as we see these youngsters with widespread peritonitis, sick from three to five days, the process in many cases has become irreversible. Nothing one does will effect a cure. That is the point that Doctor Penberthy and I have argued pro and con, and I have rather talked him around. I think to some delay, and perhaps he feels I urged him too strongly. That is the reason that I discuss this paper to-day.

I would like to mention, however, briefly, the group that we have had our greatest experience with and that is the college student. We have a large number. I do not know what our enrollment is but it is fairly large and we take care of acute appendicitis. These youngsters are supposed to have had some education, and are supposed to be getting more. They probably know as much about acute appendicitis as any group of lay people in the world. Their medical and surgical care, and their hospitalization, costs them nothing as that is all taken care of by their health service. So the economic point does not enter in. They are, of course the ideal group. There is no reason why treatment should not be perfect.

Since 1920 to the present time—I do not know the exact figures—we have operated upon them, and in various stages. Some will wait two or three days before we see them. We have operated upon them in all stages of acute appendicitis, local infection, etc., nearly 2,700. That is a rough figure. Three have died in that time. One of them died of infection and gangrene of the bladder. A second died of peritonitis. He remained home in his room and took castor oil for two or three days before we saw him. The third death occurred two weeks after the young man had left the hospital. He was cranking an automobile and died suddenly. I suspected it was an embolus, but we never had any proof because autopsy was not permitted.

Those results show what one can do, and it seems to me they show that diagnosis in an intelligent adult is not too difficult because we have made many errors but they have been compensated for by the youth and the care we have given this group.

In conclusion I would suggest to Doctor Penberthy, that perhaps the only way you and I can lower the mortality in these youngsters with peritonitis who live in our neighborhood is to urge upon the mothers that they give the youngsters less castor oil and, as Doctor Boland suggests, probably more 'pot liquor'.

DR DAVID E ROBERTSON (Toronto, Canada) I want to ask your indulgence for a few moments while I show you a few lantern slides.

(Slide) These are the records of cases coming from the Hospital for Sick Children of Toronto, January 1, 1940 to March 27, 1942, total number of appendicectomies, 1,043.

Of these, 465 were definitely acute appendicitis. No mortality in this group. Gross perforation of appendix, 115. Bacteria in free peritoneal fluid, 67. Conservative treatment in 19. Simple drainage in 14. Sulfonamide therapy, 126. Miller-Abbott Tube, 30. Deaths, two.

I thought we had only had one death at the time, but the pathologists very kindly found me a death on the medical side. This patient had been admitted to the surgical ward and had been diagnosed as, apparently, peritonitis, because he was said to have pneumonia on the same side. The Miller-Abbott tube was introduced and during the first five days it worked rather unsatisfactorily, but they did recover about 1,500 cc. After that, I find by the record, the boy was transferred to the medical side for the treatment of pneumonia, and in another four or five days he died. He was autopsied and was found to have had a ruptured appendix.

(Slide) This was the sixth day of illness, ruptured appendix, with general peritonitis.

Left-side bronchopneumonia Sulfonamide therapy throughout I might say that we use the drug intravenously On the sixth day he obviously had distinct distention

It is an extraordinary thing that it is so difficult to follow these cases carefully This lad had a tube introduced that could have been put in just a little farther, and then it would probably have passed on more quickly and gone to the proper route

(Slide) This shows the seventh day in the morning and the seventh day in the afternoon The tube is engaged in the duodenum but it was not allowed to pass on It was pushed in so that it stayed in the stomach

(Slide) At the eighth day of illness it is still in the stomach, and at the ninth day it is still in the stomach He was taken over to the medical side, and they reviewed it the boy died

I think it is obvious in this boy that whether or not the distention was the cause of his death, he did have distention, and he had the tube in for all that time in his duodenum So if the distention were the cause of his death a tube in the duodenum is not enough, and the distention down below whatever the peristalsis there is will push the gas down to the lowest point down to the point of obstruction and that distention of the wall there is what causes the reflex nervous shock, and what I believe to be the cause of death in appendicitis

The next case is a boy who came into the hospital first October a year later than this one He came in with an odd history of having been seen by a physician The physician called up and gave the history The physician had seen him the night before and the boy had a strangulated hernia which he reduced The child was still ill during the night and the next morning the physician was called again the boy again had a strangulated hernia on the same side which he had reduced The boy was sent to the hospital He obviously had a general peritonitis His condition was not fit to warrant an operation for a few hours until he was put in better condition He was then operated upon, and found to have a ruptured appendix

Thinking this boy might have a ruptured intestine from manipulation of the hernia he had a rectus incision He did well for a few days and the next I heard the resident told me the boy had died Well I demanded an inquiry When a case of appendicitis in a child dies, I believe it is some person's fault This boy should not have died

Looking back at his record I find this picture (Slide) This boy has marked distention A tube is put in crammed in The tube was left in 18 hours and nothing came out of it Three hours before death they got 250 cc of fluid out through the tube

Those are the two deaths we have had I think they were just due to neglect and misunderstanding of the problems involved Both of these boys had sulfonamide therapy I have not believed for a very long time that death in appendicitis is due to bacterial infection or intoxication I think it is a death that generally occurs about the eighth or ninth day is due to distention Looking back over the days when we operated freely on these cases, I recall that distention was the factor they all had, the common factor they had before they died So I believe that death is due to distention, but it is very difficult to make a resident appreciate that

I have established the custom of seeing every case of this type every day The resident said a few days ago Such-and-such a child is all right but he vomited yesterday I said, "Why did he vomit?" "Oh he just vomited He's all right" I examined him, and he did not have any obvious clinical distention but the next picture is this one (Slide) This was the boy who vomited once five days after operation The introduction of a Miller-Abbott tube decompressed him and the boy is well I think we should critically examine our patients postoperatively

In our deaths from appendicitis we should not let any of them be buried or take the pathologist's report as to the condition of the organs, but we should get a true understanding of the distention after the patient's death

DR ROBERT ELMAN (St Louis Mo) I just want to add two points from the basis of my experience at St Louis Children's Hospital There are two nonoperative procedures which I think are very important only one of which has been mentioned by Doctor Penberthy that is, the use of plasma transfusions in amounts which are really large amounting to about 10 to 20 cc per kilo

Dehydration very often is difficult to correct where there is great loss of plasma into the wall of the bowel and general peritonitis not to mention the peritoneal cavity itself

The second point, is the use of oxygen inhalation immediately after the operation, whether the patient is cyanotic or not. In that way, in the very seriously ill patients anoxia is controlled even before it develops. In many of these very sick patients the oxygen was given to the patient on his way back from the operating room to his room, and he was kept in the oxygen tent for several days.

The use of chemotherapy as well as gastric suction, in our experience, has also resulted in a very marked reduction in mortality. It has also shortened the period of delay, which I think is justified in these very seriously ill patients.

Another factor, the intraperitoneal introduction of sulfanilamide has permitted us to close a great many of these cases of general peritonitis which we would not have cared to do in previous years.

DR GROVER C PENBERTHY (closing) I am sure we are all agreed on the early diagnosis and the early operation being essential. I am sorry Doctor Collier misunderstood me. I question very much that he could contribute to my mortality. He was just being facetious. He has done pioneer work, and I am sure we are all agreed with him on the delayed operation.

I think Doctor Robertson and Doctor Ladd are to be congratulated on their mortality rates.

Relative to oxygen therapy I had to omit some of my paper, Doctor Elman. I am glad you brought that point up, because in addition to the good surgery and the plasma, oxygen therapy is a great help, especially in the child who is tremendously distended.



PUBLISHING AND THE WAR

Perhaps the most striking feature of the present-day European medical periodicals including the English publications, is that their articles are at least 50 per cent shorter than in the pre-war years. Either the editors must want to save paper, or the authors cannot summon up sufficient mental concentration to write articles of average length. Style has changed also, words are more carefully selected and their subject-matter, mostly related to one or another phase of war medicine or to public health, is discussed rather more clearly than in former years. Illustrations are seen only occasionally, owing to increased difficulties of printing and engraving, as well as to the high cost of publishing. As far back as the early part of 1941, most of the English medical journals contained announcements by their editors that the illustrations would have to be paid for by the author himself.

One wonders how many medical journals which have long been familiar to us still survive in the so-called Axis countries. We hear almost nothing from Belgium and Holland, and very little from occupied and unoccupied France. In the late November issues of the *Schweizerische medizinische Wochenschrift* are to be found a few abstracts from the French *Presse Medicale*, the *Deutsche medizinische Wochenschrift* and the *Munchener medizinische Wochenschrift*, so we know that they are still in existence, notwithstanding severe military censorship. No doubt many of our favorites have ceased publication entirely. Many editorial offices doubtless have been forced to migrate from one city to another.

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CLOSURE OF ILEOSTOMY IN ULCERATIVE COLITIS*

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THE SURGICAL TREATMENT of ulcerative colitis has been a recent development with sporadic cases operated upon previous to 1930. During the last decade there has been much interest and progress. The problem confronting surgeons at the beginning of this period was first, to determine what patients could be benefited or saved by surgery, and second, to convince internists under whose care these patients naturally fall, that surgery should not be used solely as a last resort. Through the work of McKittrick, Cave, Stone, Ladd, T. E. Jones, Lahey, the author and others, it has now been accepted that good results follow the employment of ileostomy, partial colectomy, and total colectomy, and that other operations are ineffective and should be discontinued. The medical treatment of ulcerative colitis has been shown to be unsatisfactory in approximately one-half of all cases. Kieffer,¹ in a report from the Lahey Clinic, found that patients who had been under medical treatment and followed for five years or more gave unsatisfactory results in 43 per cent. Ileostomy has been necessary in many of these cases. In spite of improvement in the surgical treatment, there has been no general acceptance of definite indications for ileostomy or uniformity in the time that ileostomy has been elected.

This paper will present our indications for ileostomy and recommend early ileostomy in patients with severe ulcerative colitis in order to obtain the earliest possible remission before irreversible structural changes in the colon occur. Early ileostomy is urged so that the ileostomy may be disconnected, restoring the continuity of the intestinal tract in some patients. There has been a long period of trial for medical management. There has been sufficient experience with ileostomy in late cases to know what results can be expected and in these cases ileostomy must be permanent. Early ileostomy and later closure of the ileostomy has not been given a trial in adult cases. At the Children's Hospital in Boston, Ladd and Gross² have closed the ileostomy of seven children. Stone³ reported the closure of five cases in 1929.

Both internists and surgeons have hesitated to advise ileostomy since so doing, in the past, has accepted a permanent fistula of the small intestine. Those not familiar with the management of ileostomy in these cases frequently consider it an intolerable situation, and one that is inconsistent with productive activity. That this is not the case has now been established.³ Nevertheless, if an ileostomy could subsequently be disconnected with safety and without serious recurrence of the disease, this would constitute an important forward step. It should be emphasized, however, that an attempt to restore intestinal continuity by anastomosis of the proximal ileum to a portion of the

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large intestine involved with ulcerative colitis, either in the infective or healed state, should be condemned. In one of Doctor Lahey's early cases in whom a satisfactory remission was obtained but rectal stricture resulted, ileostomy was taken down elsewhere, anastomosing the ileum to the sigmoid colon, against his advice. An operative death followed because of peritonitis. Even though obstruction is not present, the anastomosis utilizing involved colon is almost certain to leak.

We have previously stated in a number of communications⁴ that once an ileostomy is accepted it must always be maintained. There are additional reasons why we previously considered an ileostomy as permanent. In our earlier cases it was performed only in the complicated, advanced cases, usually with marked cicatricial changes in the colon. Furthermore, as soon as the ileostomy is made an even further contraction of the colon occurs from disuse. With clinical remission and healing of the colon as the result of ileostomy, contraction is inevitable. For this reason we do not believe there can be any appreciable change in the policy regarding ileostomy for advanced cases. As previously stated, there has been no clinical trial of disconnecting ileostomies in adults. For this reason we decided to take favorable cases in which ileostomy was definitely indicated, and if satisfactory response was obtained, disengage the ileostomy. After demonstrating this in favorable cases (Cases 1-5), less favorable and unfavorable cases were then tried (Cases 6-9), but no anastomoses of the involved colon have been performed.

INDICATIONS FOR ILEOSTOMY

In order to be able to review critically cases in which ileostomies have been taken down, it is necessary to outline our indications for ileostomy in ulcerative colitis, since obviously if ileostomy were selected for mild cases, closure could be employed with fair frequency. In these, however, medical treatment is usually satisfactory. The indications for ileostomy in our clinic are as follows: (1) Acute fulminating cases, either in a first attack or with recurrent acute attacks, (2) medical failures, including those patients who are incapacitated, (3) massive hemorrhage, (4) subacute perforations, abscesses, peritonitis or fistulas, (5) obstruction, and (6) polyposis including those cases with possible malignancy.

SELECTION OF CASES FOR CLOSURE

We have used three means in selecting cases for closure of ileostomy: (1) We have felt that a clinical remission of symptoms should be maintained for an appreciable period. (2) The inflammatory process must be shown to have healed and be inactive, as observed by sigmoidoscopic examinations. The mucosal surface may still be granular or scarred and may even bleed somewhat on manipulation with a swab, yet any evidence of active infection eliminates the case from closure. (3) The colon must be shown to be distensible by means of a barium enema or double contrast air enema (Figs 1 and 2). Some haustral markings should still be demonstrable, at least in

FIG 1



FIG 2

FIG 1—Case 2 *a* The full barium enema taken November 10, 1938 six weeks after ileostomy. The sigmoid, rectosigmoid, and right colon distend readily. The remainder of the colon is narrowed but with suggestion of haustral markings. This is chiefly the contracture of disuse as a result of ileostomy.

b The empty film shows excessive emptying and spasm, with some irregularity of the mucosa. The sigmoidoscopic examination was negative at this time. This is a favorable situation for closure of ileostomy.

FIG 2—Case 2 *a* and *b* The full and empty barium enema taken February 23, 1939, three months after closure of ileostomy. Full distensibility and flexibility are demonstrated. The ileocecal valve is incompetent.

the film taken after evacuation of the enema. Haustral markings may be absent in the full enema. An adequate lumen and absence of any local areas of obstruction must be demonstrated. The mucosal pattern should not show pseudopolypoid or too irregular an outline. The following case report will well illustrate the type of serious case of ulcerative colitis in which closure has been carried out (Case 4).

Case Report—This patient, a man, age 25, first came to the clinic on February 19, 1934, to be examined for possible heart trouble. He was found to have a small, right,

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indirect inguinal hernia. No heart disease was found. In August, 1934, he reported that he was getting along well except that the hernia was larger. He returned to the clinic in July, 1937, because of difficulty in swallowing. At this time, a complete gastroenterologic study was carried out, and a diagnosis made of cardiospasm and nervous exhaustion. Complete examination of the blood, the Hinton test, gastric analysis, fluoroscopy of the stomach, gallbladder test and barium enema were all negative. There was no evidence of ulcerative colitis on roentgen examination after a barium enema.

In January, 1940, the patient had severe low abdominal pain, rectal bleeding and fever. Three weeks before his admission to the hospital hemorrhoidectomy was performed, following which he had severe intestinal cramps and passed many liquid, bloody stools daily. He had been on a strictly limited diet, chiefly of carbohydrates, for seven months. The diagnosis was ulcerative colitis, thrush, and avitaminosis. Agglutination tests for undulant fever and dysentery were negative. The Widal reaction for typhoid and paratyphoid disease was negative. Stool cultures on repeated occasions showed a large amount of yeast, *B. coli*, *Staphylococcus aureus*, and streptococci. An ischio-rectal abscess was present, and this was drained the following day. The culture from the pus showed *Staphylococcus aureus* and *B. coli*. He continued to pass a large amount of pus and blood by rectum. Multiple skin furuncles and ulcers of his mouth developed. The high fever persisted, three blood cultures were negative. He was considered too ill to examine by means of a barium enema. Proctoscopy showed the typical findings of acute ulcerative colitis. Treatment with sulfathiazole did not alter his fever or symptoms.

Ileostomy was performed February 7, 1940, without abdominal exploration. An immediate decompression of the ileum was effected. The patient received a blood transfusion on that day, on March 11, and on March 16. Pain developed in the right lower quadrant, followed by the production of an abscess, and later a pelvic abscess developed, which ruptured spontaneously into the bowel. On May 29, a roentgenogram of his colon showed little change in the bowel except in the rectal region. After another blood transfusion he was discharged from the hospital in greatly improved condition on July 19, four and one-half months after admission.

The patient was reexamined on October 19, 1940, at which time there was a sinus around the ileostomy. On proctoscopic examination there seemed to be adequate sphincter control, the mucosa was entirely normal. There was no discharging pus. A barium enema showed good flexibility. The mucosal pattern was found to be within normal limits throughout (Fig. 3).

On October 31, the ileostomy was resected, draining a small chronic abscess of the abdominal wall, and a side-to-side anastomosis of the terminal ileum was performed. Sulfanilamide powder was placed in the wound and the peritoneal cavity. The colon appeared to be within normal limits. There were congenital polyps of the distal small intestine.

On December 20, 1940, after a barium and air enema, roentgenologic examination was negative (Fig. 4). On November 10, 1941, more than a year after operation, the patient weighed 176½ pounds, was well, and had no bleeding. Rectal and proctoscopic examinations gave negative results. He had one formed stool a day. The abdominal wound was firmly healed.

In January, 1942, while working in an airplane factory, the patient was badly burned about the face, hands, and shoulders in an explosion, but he made a good recovery.

March 25, 1942, he had recovered without recurrence of the ulcerative colitis.

CLINICAL DATA

We have closed the ileostomy in nine patients. The first patient was a boy 11 years of age whose ileostomy was closed in 1935 (Case 1). He had a mild recurrence the third week after closure but has been quite well since, for a period of over six years. Our second case was a man, age 38 (Case 2),

FIG 3

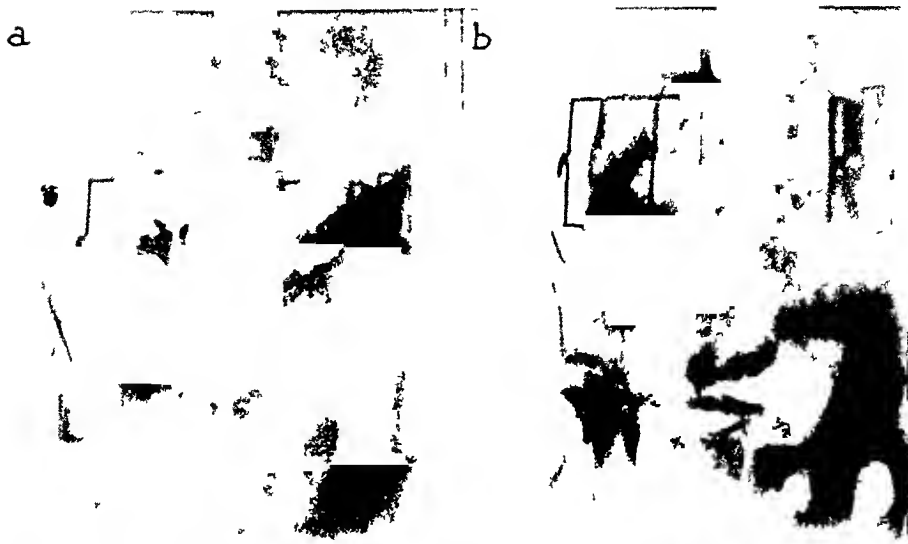


FIG 4

FIG 3—Case 4. *a* and *b* The full and empty barium enema taken October 15, 1940, eight months after ileostomy. The findings suggest complete healing with the contracture of disuse due to ileostomy. The proctoscopic examination was negative at this time.

FIG 4—Case 4. *a* and *b* The full and empty barium enema taken December 20, 1940, approximately two months after closure of ileostomy. Except for a more rapid emptying time and spasm, the findings approach those of a normal colon.

with a very acute, fulminating form of ulcerative colitis as a first attack. His ileostomy was closed in November, 1938. He was well for two years and three months, and then had a moderate recurrence at the time of an acute upper respiratory infection. Since that period when he had medical treatment he has been well. During 1939, 1940, and 1941, seven additional cases have been closed. During this period of three years, 50 ileostomies were performed, with five deaths, an operative mortality of 10 per cent. In the group of 45 patients who survived the operation of ileostomy, seven have been closed, or 15.5 per cent of those surviving operation and 14 per cent of all ileostomies during this period. Twelve patients still have their ileostomy.

and are being carried along under medical observation. Some of these are being followed with the expectation that their ileostomies may be closed.

In our group of nine patients, there was one child of 11, who was the youngest of the group, the oldest was 56. The ages of the remainder were 19, 20, 21, 26, 31, 38, and 44. The ages of these patients agree with the general age-group of patients suffering with ulcerative colitis, those of a young adult group. Seven patients were men and two were women. I think without question that the large group of males is partly due to insistence on their part that the closure be done so that they could return to work without ileostomy, since the sex distribution of our cases of ulcerative colitis is about even.

TABLE I

Case	Age and Sex	Duration of Colitis	Duration of Medical Treatment	Indication	Date of Ileostomy	Condition of Colon	Date of Closure	Ileostomy Present	Result
1	11 M	5 mos	1 mo	Med failure	11/7/34	Favorable	8/13/35	9 mos	Well (mild recurrence 3 wks after closure)
2	38 M	5 mos	7 days	Med failure	8/23/38	Favorable	11/22/38	3 mos	Well (mild recurrence February, 1941)
3	21 F	2 mos	5 days	Hemorrhage	1/26/39	Favorable	6/21/39	5 mos	Very well
4	31 M	3 wks	7 days	Acute fulminating, abscesses, fistula	2/7/40	Favorable	10/31/40	8 mos	Well
5	56 M	5 wks	18 days	Med failure	5/17/40	Favorable	11/26/40	6 mos	Well (recurrence, October, 1941)
6	44 M	4 mos	36 days	Abscess, fistula	12/2/40	Unfavorable	5/16/41	5 mos	Improved but several stools daily
7	20 F	3 yrs	21 mos	Med failure	1/10/39	Unfavorable	5/26/41	28 mos	Failure from obstruction, malnutrition, new ileostomy 3/24/42
8	19 M	3 mos	1 mo	Generalized peritonitis	4/9/40	Unfavorable	10/28/41	18 mos	Improved but many stools daily
9	26 M	6 yrs	3 mos	Reg ileitis, recurrent acute	9/11/40	Unfavorable	11/8/41	14 mos	Failure from colitis, new ileostomy 2/9/42

Only one of our nine patients had had ulcerative colitis for under one month. This was an acute case that had had ulcerative colitis for three weeks and been under treatment for seven days. Many patients with the acute, fulminating form die from their disease even though ileostomy is accepted early. Six of the patients had had their disease one to six months. They represent a group of serious cases and yet have not had their disease so long that the colon had been unalterably changed. One patient had had ulcerative colitis for three years and was a definite failure after closure, as was the patient who had had ulcerative colitis for six years.

A consideration of the indications for ileostomy in this group of nine patients is of interest. Referring to our group of indications for ileostomy we find that ileostomy was elected for the following reasons: (1) Acute, fulminating, one, (2) medical failure, four, (3) hemorrhage, one, (4) infection, two, (5) obstruction, one, and (6) polyposis or malignancy, none.

In addition to determining the duration of the ulcerative colitis, it is important in this group of cases to know the duration of the medical treatment, which was as follows: One to seven days, three; one to four weeks, three; one to three months, two; 21 months, one. The latter case was a failure.

As we first considered the possibility of closure of ileostomy, we felt that a long period of time should elapse before considering closure. These patients had their ileostomy from three to 28 months, the latter one being a failure. Four patients had ileostomy for six months or less, two patients had ileostomy for six to 12 months, while one each had their ileostomy for 14 months, 18 months and 28 months. The patients having ileostomy for 14 months and 28 months were failures, while the one having it for 18 months was unimproved after closure.



FIG 5—Case 8. *a* The full barium enema taken 18 months after ileostomy. There is foreshortening of the colon with both flexures drawn downward with little flexibility or distensibility. The mucosal outline is irregular.
b The empty film shows rapid emptying of the distal half of the colon with retention of barium in the proximal colon. This is an unfavorable case for closure.

RESULTS

There was no operative mortality in this group. The fact that restoration of their intestinal tract was accomplished by anastomosing normal ileum and not any part of the bowel involved with ulcerative colitis is, we believe, responsible for the fact that these cases were closed without complications or mortality.

The results of ileostomy in this group of seriously ill patients were good. In other words, clinical remission was obtained or the symptoms for which ileostomy was elected, were relieved in all nine patients. However, when the ileostomies were disconnected, the results were by no means as satisfactory. Two patients have had complete relief of their disease. One of these was a patient who was operated upon for hemorrhage (Case 3), and the other was a patient who had pelvic peritonitis from a subacute perforation (Case 4). Three patients had a mild recurrence on one occasion and with further

FIG 6



FIG 7

FIG 6—Case 9 *a* and *b* The full and empty barium enema taken July 1, 1940, after a modified Mikulicz resection of the ileum and a portion of the right colon for regional ileitis. There is no evidence of ulcerative colitis at this time.

FIG 7—Case 9 *a* and *b* The full and empty enema taken October 5, 1941, 13 months after ileostomy. There is marked contraction, foreshortening, irregular mucosal outline, and rapid emptying. This is an unfavorable case for closure and required a second ileostomy.

medical treatment have remained well (Cases 1, 2 and 5). We consider these five patients to have a satisfactory result. Two patients have continuing bowel symptoms without recurrence of fever, but are able to work (Cases 6 and 8). Both of these patients should be considered to be unimproved so far as ileostomy closure goes. Probably ileostomy was responsible for obtaining their clinical remission, but because of cicatricial changes in the colon (Fig 5), they have mild, obstructive symptoms or have frequent bowel movements daily. Two patients had complete failures and have had

a new ileostomy performed. One of these had had the disease for three years, and the ileostomy was kept open for 28 months (Case 7). The other patient had had trouble for six years, and the ileostomy was kept open for 14 months (Case 9). One failed because of definite obstruction and malnutrition, without evidence of active infection, while the other failed because of definite recurrence of ulcerative colitis.

A consideration of these cases demonstrates clearly that the best results can be anticipated in those patients in whom ileostomy has been done relatively early, since the favorable results in this group of nine patients were clearly in a group of cases in which early ileostomy was decided upon. A patient, recently operated upon, demonstrates this quite well. She had been observed for a period of two years, during which time she has had two long periods of medical treatment in the hospital. The barium enema at the time of the initial treatment (Fig 8 a) shows an enlarged, dilated colon, with a smooth outline. After evacuation of the enema, spasm and contraction were seen in the distal half of the colon, with satisfactory haustral markings in the proximal two-thirds of the colon (Fig 8 b). Two years later, when she had very unsatisfactory results from medical treatment, the barium enema showed marked contraction and foreshortening of the colon, with both splenic and hepatic flexures drawn downward. There were no haustral markings either before or after the enema and the mucosal pattern was definitely irregular (Fig 9 a and b). Since we did not elect ileostomy two years ago, we have lost any chance of restoring continuity in this patient. Ileostomy was performed March 24, 1942. There will be further contraction to produce the typical "lead-pipe colon" in this patient within three to six months after ileostomy. If she still continues to have symptoms, total colectomy will be necessary. The clinical story and roentgenograms in this patient demonstrate clearly our reasons for recommending early ileostomy in serious cases of ulcerative colitis.

Any patient who is not doing well on medical treatment, continuing to lose weight, run fever, and with excessive stools, should have ileostomy. Patients with the acute, fulminating form of the disease who do not respond to medical management within the first five to seven days should have ileostomy. In the acute, fulminating cases ileostomy should be done in all of them whether it is the first attack or a recurrent acute attack, unless they have a rapid response to treatment. In our group of nine patients, closure of ileostomy was possible in patients who were done as recommended. We believe in spite of a limited experience that definite evidence has been presented to show that closure of ileostomy can be done in specially selected cases where ileostomy has been done reasonably early. Approximately 25 per cent of all cases of ulcerative colitis will require surgical treatment. Closure seems possible in approximately 10 per cent of operated cases. If the indications for ileostomy are extended and if ileostomy is decided upon earlier, this figure may be increased.

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FIG 8



FIG 8—*a* The full enema of the colon of a young woman with a severe, first, acute attack of ulcerative colitis. The outline of the mucosa is smooth, with a suggestion of haustral markings. There is no contraction.
b With the empty film there is excessive emptying of the distal half, with retention of barium in the proximal half of the colon. This is the ideal roentgenogram finding for early ileostomy with a chance of subsequent closure.
 FIG 9—*a* and *b* After recurring acute attacks and several periods of medical trial utilizing all conservative means the colon is now foreshortened and contracted with a smooth outline. Ileostomy was necessary because of medical failure. There is now no prospect of subsequent closure.

SUMMARY AND CONCLUSIONS

The present status of the surgical treatment of ulcerative colitis is reviewed, and the surgical indications for ileostomy are presented. Closure of ileostomy has been carried out in nine patients, with satisfactory results in five. Two continue to have symptoms sufficient to make

them unsatisfactory, and two were complete failures, and a second ileostomy was required. There were no operative deaths.

Early ileostomy for patients with serious ulcerative colitis is recommended when medical treatment fails, in order to obtain the earliest possible remission before irreversible structural changes in the colon occur. It is in this group that later closure of the ileostomy can be considered.

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DISCUSSION—DR HENRY W. CAVE (New York). To condemn an individual particularly the young to permanent ileostomy is a serious decision. We all recognize that the mortality after ileostomy is approximately 20 per cent due to the fact that both the physician and the gastro-enterologist knowing the disease to be a cyclically recurring one with phases of convalescence and quiescence hope for a remission. Thus they wait and wait until the call for emergency surgery in desperately ill patients is sent out after hemorrhage, septic fever, dehydration and total lack of any type of resistance to infection have taken their toll.

Doctor Cattell no doubt realizing the profound morbidity of this disease and the discomfiture of an abdominal fecal fistula is convincing. I feel, in his presentation that early ileostomy is justified and that in selected cases the ileal stoma can be taken down and fecal continuity restored.

We must be cautious in advising early ileostomy only when it is beyond question that the patient is suffering from a true ulcerative colitis, as we know it and not from amoebic or bacillary dysentery, or milder form of colitis which is amenable to medical management.

To obtain "the earliest possible remission before irreversible changes have taken place" in severe ulcerative colitis the earlier the ileostomy the greater the chance of complete permanent restoration of the fecal stream.

Doctor Cattell has been fortunate in having turned over to him six of the nine patients (whom he closed later) with the disease existing for a period not longer than six months. I have had no such luck. All of the 45 patients to whom I have given an ileostomy except three (who had massive hemorrhages and who were of the acute, fulminating group and who died after ileostomy), had irreversible changes before I had been given the opportunity of diverting the fecal flow. I believe that he is right without question when he states that an attempt to restore intestinal continuity by anastomosis of the proximal ileum to a portion of the large intestine involved with ulcerative colitis either in the infective, infectious or healed stage should be condemned. Also, I am in complete agreement with his "policy regarding permanent irrevocable ileostomy for advanced cases."

I am not in accord with all of Doctor Cattell's indications for ileostomy in ulcerative colitis—particularly in reference to *massive hemorrhage*. We have had a 50 per cent mortality where we have given ileostomy to patients in the acute fulminating stage accompanied by massive hemorrhage. It is my opinion, that the mortality can be lowered considerably if by the use of papaverin hydrochloride, belladonna and repeated transfusions they can be carried through this desperate stage of hemorrhage and converted into a more chronic form.

To me, it is of especial interest to learn of Doctor Cattell's criteria for selection of cases for closure of ileostomy. The first, a clinical remission of symptoms following ileostomy, and that accompanying medical treatment should be maintained for an appreciable period. By this appreciable period, I assume he means from six to eight months.

or even longer, and I should like to ask Doctor Cattell if he has used either sulfalylguanidine or sulfasucidine in irrigating out the colon or has given orally the other sulflylonamides during this waiting period. Secondly, that the inflammatory process must be shown to have healed and to be inactive, as observed by sigmoidoscopic examination. I have found it difficult to determine accurately how inactive the process is by the use of the sigmoidoscope. So many patients seem to be in the quiescent stage and yet the slightest irritation from the insertion of the sigmoidoscope will produce bleeding, and a granular mucosal surface will exist indefinitely. Thirdly, the distensibility of the colon by means of a barium enema or double contrast air enema, and also that the haustral markings should be demonstrable "at least in the film taken after evacuation of the enema." To me, the presence of haustral markings in the entire colon after evacuation of the enema would indicate a reasonably favorable and successful closure. Needless to say, as he has stated "that if the mucosal pattern shows a pseudopolyposis or a too regular outline, closure would be out of the question." He states that one of the series of nine patients who had the disease for three years was a definite failure after closure and, also, he states that another patient, ill for six years, proved a failure after closure. It seems to me that these two failures should have been expected.

The duration of the medical management before operation was short, "one to seven days, three, one to four weeks, three, one to three months, two, 21 months, one." Ninety per cent of the patients in my own series have been treated for a much longer period. There was no operative mortality in this group of nine that he closed. May I ask what type of ileostomy was carried out? Was it divided or end-ileostomy, or was it a loop-ileostomy? It would seem to me that, particularly in the acute fulminating type, of which he had one, and of the massive hemorrhage type, of which he had one, that loop-ileostomy would be less hazardous.

In all nine of the patients ileostomy showed a clinical remission of the disease "but when the ileostomy was disconnected the results were by no means as satisfactory." Two of the patients were complete failures and had to have new ileostomies performed. Even with these failures I believe that to have had five of the nine patients with satisfactory results justified the procedure of early ileostomy and subsequent closure of the opening.

I wish to congratulate Doctor Cattell in his fine presentation, for I am sure it is a step forward in the treatment of this devastating disease. Ileostomy, at its best, is assuredly undesirable, and any method, program or maneuver that can eliminate it, is to be commended.

DR WILLIAM E LADD (Boston, Mass.) I am a little bit in the position that Doctor Oughterson put Doctor Harvey in yesterday, because Doctor Gross is looking up our data at the Children's Hospital on ulcerative colitis, but I have not been permitted to see them yet so I do not have all the data at hand.

I think we have not felt justified in undertaking an ileostomy quite as early as Doctor Cattell has. In children it is, I think, fairly difficult to group the cases into the ones that may possibly recover as the result of prolonged medical treatment and the cases that will never recover as a result of prolonged medical treatment. So we have not felt quite justified in performing ileostomy as early as some of Doctor Cattell's cases. However, I think we have established them perhaps earlier than some others have.

We have had seven cases which we have closed after leaving the ileostomy functioning for quite a long period of time, I think a good deal longer period of time than Doctor Cattell has used. I do not think we have closed any prior to the ileostomy having functioned for at least two years. I think that these seven cases that have been closed have all remained well. I know that in one case I closed 12 years ago, I had a letter from the patient two or three weeks ago, saying that she was perfectly well and asking whether we thought it was advisable for her to get married having had her previous history. I advised her to get married, and I presume she has.

There is one unfortunate case which we had that I think perhaps is quite as important as the clinical observation on the cases that we have closed. This case was a boy of about six, who had an ileostomy, which had been open for about two years. I had examined him by the sigmoidoscope and I thought he was a suitable case for closure, and I had made an appointment for him to come into the hospital to have it undertaken. In the interim he developed a volvulus from which he died. We had a postmortem examination, and a very careful examination of the colon showed it to be completely healed. It seems to me that this is really a very important piece of data.

Now I think there may be some of you who are not familiar with the fact that this

disease occurs in very early life at times We have had three cases in the first six months of life Of these, one had an ileostomy which was closed, and I think that was about three years ago That child is quite all right One has had an ileostomy, and on frequent examinations we have not felt justified in closing it, as there is still evidence of the disease persisting in the colon The third was kept on our medical ward and was not correctly diagnosed by our medical colleagues, and died The postmortem examination showed a typical ulcerative colitis with perforation, and death from peritonitis

DR FRANK K BOLAND (Atlanta Ga) I would not rise again, except for the reference which was made to what I said about ulcerative colitis in the Negro

It is true that the colored race had very few cases of this condition As a matter of fact, I have seen only two or three in a long period of time But I am familiar with two cases of ulcerative colitis which apparently were cured by one of the sulfonamide drugs, called by our friend, Doctor Gage 'sulfa-cure-all drugs' That seems to be a good name I did not think that was so important but when I heard from one of the most eminent colon surgeons in our country that the use of these drugs had almost eliminated the necessity for operation I felt that something new was here and that is the reason it was mentioned in the paper

I would like to say in this connection a word about these drugs I think there are two things which should be considered in evaluating a drug or any procedure and that is not only the number of cases in which you have used it but also the length of time which has elapsed since the procedure came into use

For instance, you all recall how enthusiastic we were in World War I about the use of the Carrel-Dakin treatment We thought that was fine, and it did seem to be fine But I heard some gentlemen recently who had treated and seen some of the patients at San Francisco who had come from Pearl Harbor, tell the valuable wonderful results of sulfathiazole treatment of wounds Several of them seemed to think We will not have to use that Carrel-Dakin treatment any longer I hope they will not be saying that 20 years from now about the wonderful drugs we seem to have to-day

Our President is very fond of telling a story to drive home a point and I have a little story I think illustrates the error of drawing conclusions from too small a series of cases In the days of typhoid fever when we had perforations and hemorrhage a young physician had in the ward an Irishman who was in a very low state of typhoid fever, and it seemed that he was going to die As you remember the patient with typhoid fever was not fed anything in those days This Irishman was very hungry Seeing a big plate of cabbage on the table between him and another patient he reached over and took it and ate all the cabbage The young doctor knew his patient was gone but strange to say the patient immediately got well

A little later the same young physician had a Swede in the ward with typhoid fever, and he reached about the same condition the Irishman had been in Remembering the luck he had had with the Irishman's eating cabbage, he gave this Swede some cabbage and the Swede immediately died

Then the young doctor wrote a paper on the use of cabbage in the treatment of typhoid fever, and his conclusions were that cabbage in typhoid in an Irishman was a wonderful thing but in a Swede it was not worth a damn

DR RICHARD B CATTELL (closing) I appreciate the discussion including Doctor Boland's reply I think I might comment on it first and say that I think his caution with regard to any interpretation of results in a small series of cases such as this certainly must be approached with great prudence

Dr Cave raised the question with regard to hemorrhage and how serious these cases are We feel that only ileostomy offers any possible prospect of surgical help in these cases We have employed actual irrigations with sulfonamides in only a few We have used sulfanylguanidine and other sulfonamides by mouth and our results chiefly done under Doctor Kiefer's direction have not been as satisfactory as many that have been reported

With regard to the other question of Doctor Cave as to the type of ileostomy, we have established a divided ileostomy in all of these cases

In the text of my paper you will find the reference to Doctor Ladd's and Doctor Gross's series of closures in seven children I was familiar with this work and I think that it was largely instrumental in encouraging us to try this in adults I think Doctor Ladd's results are better than our own I believe that one of the reasons why the percentage of our number of recurrences is high is because we tried it in bad as well as in good cases

EXPERIENCES WITH THE SURGICAL MANAGEMENT OF DIVERTICULITIS OF THE SIGMOID*

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A SURVEY of the literature and of experiences with the management of diverticulitis of the colon at the Massachusetts General Hospital during the past 15 years indicates that this is a comparatively rare disease. It is the result of inflammation in and about outpocketings from the bowel. These most frequently appear to consist of mucosal pouches which protrude through the muscularis, presumably the result of pressure from within, probably acting in conjunction with some congenital defect in the muscular layer (Mayo, Wilson, and Giffin [1907]). This condition, known as diverticulosis, is rare, for Rankin and Brown (1930) found evidence of it in 0.3 per cent of 765,795 patients subjected to roentgenologic examination. Time is apparently an important factor, for if the age of the patient is taken into consideration, it would appear that approximately 5 per cent of people who are age 40 or over will have diverticulosis (Brown [1939]). It is not surprising, therefore, to find that diverticulitis is rare in the younger age-groups. It begins to make its appearance in the fourth decade of life and is maximal in the sixth (Table I). It is also apparent that males are affected more commonly than

TABLL I
DIVERTICULITIS

Age	No. of Cases†
20-29	1
30-39	24
40-49	86
50-59	131
60-69	105
70-79	19
80-89	3
Total	369

* Graham (1937), Brown (1939), Eggers (1941), and M. G. H. (1942).

females, the ratio being 1.6 to 1. This is particularly apparent in those patients who develop spontaneous bladder fistulae, where the ratio of males to females increases to 8.5 to 1 (Table VI).

The distribution of diverticula in the colon is of interest, as this has a bearing upon surgical complications. It is apparent that the sigmoid is involved more frequently than any other segment of the large bowel and the rectum least frequently. The sigmoid contains diverticula in 75 per cent of cases,† and the rectum in 2.4 per cent. Between the sigmoid and the cecum,

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942.

† Spriggs and Marxer (1927), and Brown and Marcley (1937).

the incidence of diverticula in the various segments of the colon decreases steadily. All segments of the bowel are occasionally involved (14.4 per cent). One might, therefore, expect that, on the law of chances, surgical complications would occur most frequently in the sigmoid. This appears to be the case, in fact, they rarely occur in any other segment. During the 15-year period, in which the 64 cases included in this report were operated upon for diverticulitis of the sigmoid, there were only two other cases subjected to surgery for complications of diverticula in other portions of the colon. One involved the cecum, and the other the ascending colon. In the latter instance, actinomycosis was also present. D. F. Jones (1930) stated that he had seen but one surgical complication of diverticulosis above the upper end of the sigmoid and that was in the cecum. This indicates that other factors which affect the sigmoid in particular, such as a narrow lumen, stasis, and solid fecal material may be important.

The sigmoid is also the most frequent site of carcinoma of the colon. Allen and Welch (1939) found that in a series of 634 carcinomata of the large bowel, not including the rectum, the lesion was situated in the sigmoid in 53.9 per cent. This probably is the reason why there is an association between diverticulitis and cancer, rather than that the former favors the occurrence of the latter. This appears to be the conclusion of most who have commented upon this matter in the more recent literature, Abel (1935), Brown and Marckley (1937). Certain statistical data also supports this viewpoint, as Rankin and Brown (1930) found diverticula associated with cancer in only four of 679 carcinomata of the bowel, an incidence of 0.6 per cent, and cancer associated with diverticulitis in four of 227 cases, an incidence of 1.8 per cent. The latter figure is lower than that reported by Eggers (1941), who found the incidence to be 6.1 per cent. On the other hand, this figure was less than the incidence of carcinoma of the sigmoid detected in a series of 428 consecutive barium enemata, which Eggers (1941) found to be 7.2 per cent. In this same series of roentgenologic examinations, the incidence of diverticulitis was 4.2 per cent.

The differential diagnosis between diverticulitis and cancer has been a topic for some discussion, particularly with regard to bleeding as a symptom and the value of roentgenograms as a diagnostic aid. Considerable evidence is available upon the former question, and indicates that a history of bleeding was present in 15.7 per cent of 568 patients* known to have diverticulitis. Of 309 cases† known to have diverticulitis in which the incidence of cancer and bleeding were both recorded, the incidence of cancer was 2.9 per cent, and of bleeding 16.5 per cent. With regard to the value of the roentgen ray in differentiating between the two lesions, Schatzki (1940) stated that the differential diagnosis is easy in most, difficult in some, and impossible in a few cases. Because of the fact that the symptoms, the signs, the age of the patient, the area

* Judd and Pollock (1924), Spriggs and Marver (1927), Rankin and Brown (1930), Ochsner and Bagen (1935), Eggers (1941), and M. G. H. (1942).

† Rankin and Brown (1930), and Eggers (1941).

of the bowel involved, the roentgenologic findings, and the gross appearance of the lesion at operation may be quite similar, it seems clear that excision of the involved segment of the bowel is the only certain answer to this question. This was the reason for resection of the sigmoid in eight (24.2 per cent) of the 33 cases included in this report. No case in which cancer and diverticulitis were associated in the same segment of the bowel is included in this series. In one case, a small, low, nonobstructing carcinoma of the rectum was present, and is included because it was felt that it had no obvious connection with the perforated sigmoid with abscess formation. Benign polyps were found in two of the 33 resected specimens.

The question arises as to how frequently patients with diverticulosis of the sigmoid develop diverticulitis. Some statistical data bearing upon this point indicates that roentgenologic evidence of diverticulitis was present in 25.1 per cent of 2,400 cases^{*} having diverticulosis. Brown (1939) believes that as many patients with diverticulosis probably have mild attacks of diverticulitis and are not roentgenographed, that a more likely estimate would be 10 per cent. It is likewise impossible to estimate accurately the number of patients with diverticulitis who require surgical intervention. From reports in the literature dealing with both the medical and surgical management of this lesion, it was found that 28.5 per cent of 1,332 cases[†] coming under observation were operated upon for one reason or another. Here again, this figure is probably too high and it would seem more likely that about 10 per cent of all cases of diverticulitis require operation. This is in keeping with the experiences of Brown and Marcley (1937) with the medical management of this disease, in which they state that the results were found to be satisfactory in 63 per cent of their cases and adequate in three-quarters of the remaining 37 per cent, which implies an unmanageable situation in 9.3 per cent of patients with diverticulitis. During the 15-year period which this report covers, our own experience indicates that of all patients hospitalized for diverticulitis, 64 (19.2 per cent) were treated surgically and 269 (80.8 per cent) were treated medically. Undoubtedly, there were many more cases treated medically without hospitalization. To summarize this matter briefly, it would appear that about 5 per cent of people over 40 years of age have diverticulosis. Graham (1937) has estimated that this means about 12 in 250 patients over 40 will have diverticulosis and one in 250 will have diverticulitis. If we assume that one in ten cases with diverticulitis will require operation, this means that a surgical problem will arise in approximately one in 2,500 people over 40 years of age. It is apparent that the experience of most surgeons with this disease cannot be great, and it is not surprising that the literature dealing with the results of various operations is not extensive.

* Rankin and Brown (1930), and Brown and Marcley (1937)

† Spriggs and Marxer (1937), Rankin and Brown (1930), Brown and Marcley (1937), Stetten and Abeloff (1938), Lockhart-Mummery (1938), Eggers (1941), and M. G. H. (1942)

TABLE II
MANIFESTATIONS OF DIVERTICULITIS*

	No of Cases	Perforation	Per Cent
(a) Incidence acute perforation	545	73	13.4
(b) Incidence abscess	506	60	11.9
(c) Spontaneous bladder fistula	611	90	13.1
			<hr/> 38.4
(d) Various other lesions			
Acute	} nonperforated		
Subacute			
Recurrent			
Chronic			61.6
			<hr/> 100.0

* Judd and Pollock (1924) Rankin and Brown (1930) Graham (1937) Brown and Marceley (1937) Lockhart-Mummery (1938) Brown (1939) Eggers (1941) and M G H (1942)

It is apparent (Table II) that nearly 40 per cent of the patients who come to operation for diverticulitis have either an acute perforation, an abscess, or a spontaneous bladder fistula. The incidence of these three complications appears to be about the same. An occasional case may have fistulae into other intestinal loops. About 60 per cent are operated upon for various other lesions, largely nonperforated or not obviously perforated. In many instances, the preoperative diagnosis is incorrect, and was so in 29 (45.3 per cent) of our 64 cases. Appendicitis, intestinal obstruction, carcinoma, and pelvic tumors were the more common mistakes. It is of interest that the symptoms in the majority of 156 cases¹ were of short duration, less than a month in 25 per cent, less than a year in 66.6 per cent, and less than five years in 91 per cent. This has been emphasized by Brown (1939). In our series, it was found that the first attack was severe and required operation in 48 per cent of the cases. The implication is that in cases which come to operation the disease is unusually severe or persistent.

TABLE III
MORTALITY STATISTICS*

	No of Cases	Deaths	Per Cent
(a) Acute perforation—principally drainage ± suture	42	10	23.7
(b) Abscesses—incision and drainage	43	4	9.3
(c) Bladder fistula—various operations	53	10	18.9
(d) Various lesions—various operations not including resection but including colostomy	173	17	9.8
(e) Various lesions—resection of sigmoid—all technics	181	31	17.1†

* Graham (1937) Brown and Marceley (1937) Lockhart Mummery (1938) Brown (1939) Eggers (1941), and M G H (1942)

† Mortality of various types of resection (25.0-61 per cent)

The immediate mortality is variable (Table III) and depends upon the nature of the lesion and the type of operation performed. It was 23.7 per cent for acute perforations, 9.3 per cent for abscesses and 18.9 per cent for bladder fistulae. The mortality for various operations including colostomy, appendectomy, exploratory celiotomy, cecostomy, and miscellaneous maneuvers for various lesions was 9.8 per cent. The mortality for resection by all technics for various lesions was 17.1 per cent. This has been emphasized by

* Total of Brown (1939), and M G H (1942)

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Laufman (1941) The mortality for resections by certain technics (Table IV) varied, and was 11.5 per cent for Mikulicz resections, 17.3 per cent for resection with anastomosis following preliminary colostomy, 20 per cent for obstructive resections, and 26.3 per cent for one-stage resection with anastomosis

TABLE IV
RESECTION BY CERTAIN TECHNIQUES*

Technics	No. of Cases	Deaths	Mortality
(1) Mikulicz resection Later close colostomy	61	7	11.5%
(2) Preliminary colostomy Subsequent resection with anastomosis Later close colostomy	52	9	17.3%
(3) Obstructive resection Later close colostomy	20	4	20.0%
(4) One stage resection With anastomosis	19	5	26.3%
Total	152	25	16.4%

* Brown and Marcle (1937), Brown (1939) and M. G. H. (1942)

TABLE V
LATE RESULTS—VARIOUS LESIONS

	No. of Cases	Living and Well	Living Not Well	Subsequent Death from Disease	Subsequent Death Other Cause	Unknown
(a) Various operations other than colostomy or resection*	98	45 (45.9%)	33 (33.7%)	8 (8.2%)	8 (8.2%)	4 (4%)
(b) Colostomy*	78	49 (62.8%)	12 (15.3%)	7 (9%)	8 (10.2%)	2 (2.6%)
(c) Close colostomy*	36	19 (52.8%)	14 (38.9%)	3 (8.3%)		
(d) Resections†	109	83 (76.1%)	8 (7.4%)	4 (3.7%)	8 (7.4%)	6 (5.4%)

* Brown and Marcle (1937) Lockhart-Mummery (1938) Brown (1939) Eggers (1941) and M. G. H. (1942)

† Lockhart-Mummery (1938) Brown (1939) and M. G. H. (1942)

The late results (Table V) and mortality following various operations, such as exploratory celiotomy, appendicectomy, with or without drainage, and miscellaneous operations, not including colostomy or resection for various lesions, including patients surviving suture and drainage of acute perforations and drainage of abscesses, have been collected from the literature in 98 cases. Of these, 45.9 per cent are living and well, and 33.7 per cent living and not well. The late results of proximal colostomy are given for 78 cases, of which 62.8 per cent are living and well, and 15.3 per cent living and not well. These results appear to be better as far as relief of symptoms are concerned, but the late mortality of the disease was not significantly altered being 8 to 9 per cent in each group. It is of interest to note that colostomies were closed in 36 cases. This was unsuccessful in 47.2 per cent of cases. The late results of resections of the sigmoid indicate that this is a more effective form of treatment. Of 109 cases, 76.1 per cent were well, 7.4 per cent not well, and the late mortality from the disease was 3.7 per cent.

One of the more distressing complications is the bladder fistula (Table VI). This occurs primarily in males and has already been commented upon. Certain operations, particularly direct attempts to close the fistula have not met with much success. Colostomy has been helpful, resection appears to be more effective.

TABLE VI
BLADDER FISTULA

	No of Cases	Males	Females	
(a) Sex incidence				
Brown (1939)	30	27	3	
M G H (1942)	8	7	1*	
	—	—	—	
	38	34	4	
		or 85	1	
(b) Sex incidence diverticulitis†	535	333	202	
		or 16	1	
				Subsequent Death from Disease
(c) Late results miscellaneous operations	No of Cases	Living and Well	Not Well	
Brown (1939)	10	0	6	4
M G H (1942)	1	0	1	0
	—	—	—	—
	11‡	0	7	4
(d) Late results proximal colostomy				
Brown (1939)	1	1	—	—
M G H (1942)	4	1	2	1
	—	—	—	—
	5	2	2	1
(e) Late results resection sigmoid				
Brown (1939)	12	12	—	—
M G H (1942)	3	3	—	—
	—	—	—	—
	15	15	0	0

*Previous total hysterectomy

†Judd and Pollock (1924) Stetten and Abeloff (1938) Lockhart Mummery (1938) Brown (1939) and M G H (1942)

‡Close fistula five cases

The immediate and late results of all operations, excepting resection, which were performed in 42 cases of diverticulitis are summarized in Table VII. There were four cases with acute perforation, nine with abscesses, three with bladder fistulae, and five with acute diverticulitis and early peritonitis, simulating appendicitis. The remaining 21 cases had various lesions which were less acute to chronic in nature. A mass was present in all at operation. These were nonperforated or not obviously perforated lesions. Large bowel obstruction was present in five. There were two deaths (4.8 per cent), both from general peritonitis, one following drainage of an abscess, and one following suture and drainage of an acute perforation. There were 13 immediate complications. Seven cases developed fecal fistulae, two general peritonitis, in one, a bladder fistula recurred six days after closure. One case developed major wound sepsis with separation, and one developed small intestinal obstruction.

The late result is known in the 40 surviving cases. Sixteen (40 per cent) are classed as well. Of these, six had proximal colostomies, and one, an entero-enterostomy between the transverse colon and the sigmoid distal to the lesion. The colostomy was closed in two cases. The symptoms recurred in both. No further surgery has as yet been necessary. Of the remaining nine cases in this group, three have subsequently died of other causes, two years eight

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TABLE VII
VARIOUS OPERATIONS—M G H (1942)—42 CASES
Excepting Resection—Arranged According to the Lesion

Immediate Result					Late Result			
Lesion	No of Cases	Operation	Complications	Deaths	No of Cases	Living and Well*	Not Well†	Subsequent Death—Dis- case
Acute perforation	4	Suture and drain	2	1	3	2	1	—
Abscess	9	I and D	6	1	8	2	5	1
Bladder fistula	3	Prox col (2) Close fist (1)	1	0	3	1	1	1
Acute diverticulitis	5	Append with drain (4)	3	0	5	1	4	0
Acute Subacute Chronic	2	Exp celiotomy Colos	0	0	2	0	2	0
		Exp celiotomy Biopsy Exc 1 and O Enter'ty	0	0	4	2	2	0
		Exp celiotomy Colos	1	0	7	5	1	1
		Exp celiotomy Cecostomy	0	0	3	1	1	1
		Cecostomy Obstructed	0	0	5	2	2	1
		All with mass			13 (30.9%)	2 (4.8%)	40	16 (40%)

* Two subsequent deaths unrelated cause
† One subsequent death cause unknown

months, 5 years seven months, and seven years two months after operation. Six are living and well, from seven months to 14 years after operation.

Nineteen cases (47.5 per cent) were classed as not well. Of these, 15 (78.9 per cent) have required further operation either for persistent symptoms or disease or for recurrent disease. In 11, resection was necessary. Three cases are living from two years six months to five years after operation, with persistent symptoms or recurrent attacks for which no further surgery has as yet been necessary. One patient died one year 11 months following proximal colostomy for bladder fistula. Until then his urinary tract infection persisted. The exact cause of death is not known.

Five cases (12.5 per cent) subsequently died of their disease. In one case, a bladder fistula, multiple operations were performed, including a terminal ileostomy. The patient eventually died of urinary tract sepsis and uremia, seven years six months after onset. One case died two years after cecostomy of a recurrence of his disease, further surgery being performed elsewhere. One case died elsewhere, six months after proximal colostomy of persistent sepsis. Two patients did well for six years and eight years six months after operation, and then died of recurrent disease. In one, a further operation for drainage of a recurrent abscess was performed, and death was due to general peritonitis.

A study of these results indicates that the outlook for patients with severe forms of diverticulitis is not very bright. The majority have not done well.

The sigmoid was resected in 33 cases. Eleven had had previous operations as described in Table VII. This makes the total series 64 cases. The immediate and late results are given in Table VIII. Six cases which were followed for less than one year were eliminated from the tabulation of late results. The average follow-up for the remaining 25 cases was four years six months. Fifteen cases have been followed for from one to five years, and nine for from five to ten years. The result in one case operated upon six years six months ago is unknown.

TABLE VIII
RESECTION SIGMOID (M G H 1942)—33 CASES

Lesion	Arranged according to the Lesion Immediate Result			Late Result (1-10 Yrs)				
	No of Cases	Complications	Deaths	No of Cases	Living and Well*	Not Well	Subsequent Death—Disease	Unknown
Recurrent divertis with mass	9	3	0	8	7	1	0	0
Recurrent divertis without mass with thickened mesentery	3	0	0	3	1	2	0	0
Chronic divertis with mass, ? ca	8	5	2	5	4	0	0	1
Bladder fistula	4	2	0	3	3	0	0	0
Persistent ext fistula	4	1	0	2	2	0	0	0
Acute divertis with mass	2	0	0	2	2	0	0	0
Acute divertis with abscess	2	0	0	1	1	0	0	0
Subacute and chronic divertis with persistent obs	1	0	0	1	1	0	0	0
	33	11 (33.3%)	2 (6.1%)	25	21 (84%)	3 (12%)	0 (0%)	1 (4%)

* Two subsequent deaths unrelated cause

Twelve cases were resected because of recurrent attacks of diverticulitis, eight because of chronic diverticulitis with a mass simulating carcinoma, eight because of persistent fistulae, four had acute lesions with an associated abscess in two instances, and one case had persistent obstruction due to a fibrostenosing lesion.

There were two deaths, a mortality of 6.1 per cent. There were 11 complications (33.3 per cent). Of the 25 cases included in the tabulation of late results, 21 (84 per cent) are classed as well, three (12 per cent) as not well. There have been no subsequent deaths from the disease. The result in one case is unknown. Of the 21 cases classed as well, two have subsequently died of other causes, one of a cardiac lesion four years six months later and the other committed suicide one year after operation. Until then there were no difficulties due to diverticulitis, although it appears that the many operations which had been performed upon the patient who committed suicide probably contributed to his depressed state of mind. On the whole, the results in this group of resections are encouraging, and the impression gathered from a study of these cases suggests that this form of treatment appears to offer the patient

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suffering from a severe form of diverticulitis the greatest hope for relief and appears to lessen the subsequent mortality from the disease

TABLE IX
RESECTION OF SIGMOID—EARLY RESULTS
(1) Exteriorizing Operations—15 Cases
Immediate Complications

Technic	No of Cases	Number	Nature	Deaths	No of Cases	
(a) Proximal loop only Anterior resection with closure distal stump	4	4	Gen'l perit'itis, retro-peritoneal sepsis 2	2	4	
Drainage 2 No drainage 2			Fecal fistula, small bowel obs, 1	0		
Proximal colostomy 2 Primary resection 2			Gangrene colostomy small bowel obs 1	0		
					C 4	D 2
					100%	50%
(b) Both loops Mikulicz 10 loops separated 1	11	3	Small bowel obs, 3	0	11	
Primary resection 9 (Alone 4 with cecostomy 5) preliminary cecostomy or colostomy 2						
					C 3	D 0
	15	7		2	27 3%	0%
		(46 7%)		(13 3%)		

(2) Resection with Immediate Anastomosis—18 Cases

(a) Aseptic end-to end anastomosis Prel cecostomy 3 accompanying cec'my 3	6	2	Serious leakage suture line abscess ext fistulae 2	0	6	
					C 2	D 0
					33 3%	0%
(b) Preliminary transverse colostomy Aseptic end-to end 6 aseptic lateral 1	7	1	Leakage suture line local abscess 1	0	12	
(c) Preliminary transverse colostomy Open end-to end	5	1	Leakage suture line, local abscess 1	0	C 2	D 0
	18	4		0	16 7%	0%
		(22 2%)		(0%)		
Total for all groups	33	11		2		
		(33 3%)		(6 1%)		

An attempt has been made to determine what factors play a rôle in the immediate mortality, the immediate complications, and why the late results in certain cases were not satisfactory First of all, it would appear that the technic of resection is a factor Data bearing upon this point are presented in Table IX In this, the cases are divided according to the technic employed Fifteen exteriorizing procedures are contrasted with 18 resections with immediate anastomosis All the deaths occurred in the former group, and the complications were over twice as frequent If, however, one divides the exteriorizing operations into two groups, it is apparent that in the first, consisting of four cases in which the proximal loop only was exteriorized and the distal loop closed, all the deaths and the majority of the complications occurred In the second group (11 cases) in which both loops were brought out by the Mikulicz technic, with one exception, there were no deaths, but small bowel obstruction occurred in three cases In the first group with the closed distal

loop, fatal general peritonitis and retroperitoneal sepsis occurred in two cases. In the other two, a persistent fecal fistula leading to the distal loop and small bowel obstruction for which multiple subsequent operations have been performed occurred in one, and in the other small bowel obstruction and gangrene of the colostomy resulted, necessitating further operative procedures both immediately and later. It is also of interest that in two of the four cases in this group a preliminary proximal colostomy had been performed eight and nine months previously. In both groups, intestinal obstruction occurred. This complication appears to be characteristic of exteriorizing procedures. It is possible that infection and inadequate peritonealization are factors because this technic is often employed when resecting acute and subacutely inflamed lesions.

The 18 resections with anastomosis may be divided into two main groups, first those with preliminary or accompanying cecostomy. Two of six cases with aseptic end-to-end anastomosis developed leakage at the suture line, extensive sepsis, and abscess formation. Multiple subsequent operations necessitated long hospitalization. In both, this was a near fatal complication. It would appear that neither preliminary nor accompanying cecostomy is adequate protection for this type of anastomosis performed for an inflammatory lesion. The other group consists of 12 cases with preliminary proximal colostomy. Either aseptic or open end-to-end suture was performed in 11. There was one aseptic lateral anastomosis. The same complication occurred in two cases. Of these, one had an aseptic and the other an open end-to-end anastomosis. This indicates that leakage may follow end-to-end suture whether open or closed, whether immediate or delayed. On the other hand, when proximal colostomy preceded resection this complication was not recognized clinically, but only because postoperative roentgenograms happened to be taken. In one instance, the perforation closed in one month and in the other, it practically closed in the same period of time. This demonstrates one advantage of preliminary proximal colostomy. It would appear that the Mikulicz resection or immediate anastomosis preceded by proximal colostomy are comparable as far as low mortality and similar incidence of complications are concerned. In the former, small bowel obstruction was the problem, in the latter it was leakage at the suture line with localized abscess formation. A review of the operative notes in 18 cases with immediate anastomosis and four cases in which anterior resection was performed, indicates that the Mikulicz technic could not have been used in 12 because the lower portion of the sigmoid loop was primarily involved. There probably were others as well. As it does not appear to be possible to decide with certainty beforehand which technic will be indicated, it would seem best to advocate preliminary proximal colostomy in all cases in which resection of the sigmoid for diverticulitis is to be performed if serious complications are to be reduced to a minimum.

Other possible factors which may have a bearing upon immediate complications and late results should be considered. As judged by the length of bowel removed at operation, it would seem that less extensive resections were

performed in the group with immediate leakage at the suture line. The group living without symptoms had more extensive resections, the average difference being 4.3 cm. This impression is also gathered from a study of such post-operative roentgenograms as were available. The majority of the patients who had either leakage or who were living with symptoms had end-to-end anastomosis of which six of seven were of the aseptic type. Spasm, delay, and narrowing at the anastomosis were common findings in these groups, and were less frequent in patients living without symptoms. In the latter group, narrowing was present in two of nine cases, and spasm in one. Perhaps the most noteworthy finding was absence of delay at the anastomosis in all of the good results examined roentgenologically. Residual diverticula were usually present after operation in all groups.

The character of the bowel at the time of operation is undoubtedly a factor. A narrow lumen, a thick wall, and acute inflammation all seem important, particularly with regard to end-to-end anastomosis. It is also reasonable to believe that the mortality and immediate complications following the Mikulicz type of resection, comparatively safe as it is as a primary procedure, might be, likewise, reduced by a period of delay. If such is the case, the added time consumed would be amply justified. One of the principal reasons for performing a preliminary proximal colostomy is to allow infection to subside. The period of delay should be dependent upon the time required for this to take place.

A review of the pathologic specimens removed at operation showed that of 14 cases in which primary resections were performed acute inflammatory changes were present in 12. There was a time interval of 11 days to three weeks between cecostomy or transverse colostomy and resection in six cases. Acute diverticulitis was present in four. Seven weeks to three months elapsed between proximal colostomy and resection in four cases. Acute inflammation was present in three of these specimens. The time intervals in five cases between transverse colostomy and resection were three and one-half, five, five, five, and eight months, respectively. There was no evidence of acute inflammation in any of these. This suggests that the time interval should be not less than three months and probably need not be over six months. There was a time interval of six to ten months in four cases with persistent external or bladder fistula, between proximal colostomy and resection. Acute inflammatory changes were present in all. It seems reasonable to believe such would be the case as long as a fistula persisted. The interval in such cases would, therefore, appear to depend more upon the time it takes for such fistula to heal.

In this connection, it was found that external fistulae developed in seven of 17 cases in which drainage was employed in the management of acute perforation (three), abscesses (ten), and acute diverticulitis for which appendectomy and drainage were performed (four). Spontaneous healing occurred in two cases in nine weeks and 11 weeks, respectively. In five cases, the fistulae persisted and were observed for five, five, 17, 19 months, and three

years, respectively. At these times, further surgical procedures were instituted, proximal colostomy followed by resection in three, proximal colostomy only in one, and excision with transverse colostomy in one. In the three cases which were resected, the time intervals between colostomy and resection were four and one-half, five, and six months, respectively. The bowel opening was patent in every case. The external fistula healed in one case (time interval six months). One other case, with a fistula of one week's duration, was resected ten months after proximal colostomy. Both openings of the fistula were still patent. In one case, with proximal colostomy only, for external fistula of three years' duration, the external opening closed promptly. The patient also had a bladder fistula which did not heal, suggesting that the bowel opening was still patent.

No evidence of spontaneous and persistent healing of bladder fistulae was found. Proximal colostomy followed by resection was performed in four cases. The duration of the fistulae at the time of colostomy was two years, six months, four and one-half months, and three months. The time intervals between colostomy and resection were two, nine, three, and nine months, respectively. The bladder opening was closed in the first and fourth, the bowel opening in the fourth only.

Proximal colostomy only was performed in four cases with bladder fistulae. In one of these a terminal ileostomy was performed. The fistulae had been present for one, 15, one, and two months, respectively. In the third case, clinical evidence indicates that the fistula healed promptly and has remained healed for seven and one-half years. In the other three, clinical evidence suggests that the fistulae remained active for 15 months, six and one-quarter years, and six and one-third years, respectively. Two of these cases are dead, the first and third. The latter is known to have died primarily of urinary tract sepsis and uremia, and the other was known to have persistent urinary tract sepsis up to the time of death.

It appears to take not less than three months of proximal decompression by colostomy for evidence of acute inflammation in resected specimens to disappear except in cases in which external or bladder fistulae persist. In these cases, acute infection was invariably present even after ten months of proximal colostomy. External fistulae following drainage operations either healed spontaneously in three or four months or persisted up to three years. Following proximal colostomy, two external fistulae healed promptly or within six months. The bowel opening did not heal in either of these. Following proximal colostomy, three external fistulae persisted, the bowel being open in all at the time of resection four and one-half, five and ten months later. Following proximal colostomy for bladder fistulae, healing occurred within a few months in one case and did not take place in three cases for fifteen months, six years three months, and six years 4 months, respectively. From this, it would appear that a time interval of from three to six months should elapse between proximal colostomy and resection. There appears to be little to be gained in cases without fistulae by a shorter interval except where the

possibility of carcinoma exists, and little to be gained by a longer delay in patients with external or bladder fistulae which have not healed within this period of time

The length of the resected segment of bowel was short in the majority of instances. This figure is known in 27 cases, the average for the group being 13.6 cm, or 5.4 inches. In 23 cases (85 per cent), the area removed ranged from seven to 15 cm, averaging 12.3 cm. In only four cases was a longer segment removed, the measurements being 17, 17, 24, and 25 cm. In none was this done because the lesion was unusually extensive. In the first two, the purpose was to remove as much as was readily possible and still restore continuity. In the third, the bowel was unusually redundant, and still is according to postoperative roentgenograms. In the fourth, an anterior resection was performed for a low lesion thought to be carcinoma, the segment removed far exceeding the involved area. These findings confirm the statement of Spiggs and Maixner (1927), that the disease generally involves a localized area of the bowel. The reason why the disease is serious in some cases and not in others does not appear to be because it is more extensive, but rather because there is a more serious and persistent process in a localized segment of the bowel. Continuity of the bowel was reestablished in 27 (81.8 per cent) of the 33 resected cases, and judging by the operative notes, could have been restored in all, with one possible exception. When approached directly in the acute phase, the impression may be gathered that the lesion is extensive, for the inflammatory process in the bowel may reach far beyond the point of origin. When in a quiescent phase, it is generally found to be localized in extent, resectable, with restoration of continuity in the great majority of cases, and higher in location than was expected. The lower third of the sigmoid was principally involved in 12 (36.4 per cent) of 33 cases.

CONCLUSIONS

(1) The late results of operations for diverticulitis, which neither divert the fecal stream nor remove the involved segment of the bowel, were unsatisfactory in over 40 per cent of cases. In these, some further surgical procedure often was necessary.

(2) The late results of proximal colostomy were better. Unsatisfactory results occurred in about 25 per cent of cases subjected to this procedure. This operation does not appear to lower the late mortality due to the disease. It does relieve symptoms. Later closure of the colostomy was unsuccessful in over 45 per cent of cases.

(3) The late results of resection of the involved segment of the bowel were unsuccessful in approximately 12 per cent of cases. This operation appears to lower the late mortality due to the disease.

(4) The immediate mortality for resections has been high, the average being 17.1 per cent. This figure varies considerably (25-61 per cent). The immediate complications in our series were frequent (33.3 per cent).

(5) The Mikulicz operation was found to be comparatively safe, although

complicated by small bowel obstruction occasionally. The reported mortality (11.5 per cent) for the operation should be reduced if possible. Both open or aseptic end-to-end anastomosis were complicated by leakage at the suture line and abscess formation. In these, the length of the segment removed was short. Leakage was a serious matter in cases in which a preliminary colostomy had not been performed. Preliminary or accompanying cecostomy was not adequate protection for resection with immediate anastomosis. The late results of the Mikulicz operation and open end-to-end anastomosis were satisfactory. There was no evidence of delay at the anastomosis in these. In three cases with less satisfactory late results, aseptic end-to-end suture was performed. In two of these, delay at the anastomosis was found. In general, as judged by postoperative roentgenologic examination, the more extensive resections were performed in cases with satisfactory late results. Anterior resection with closure of the distal segment was found to be an unsatisfactory technic.

(6) The inflammatory process is generally situated in the sigmoid, and confined to a localized area. Resection with reestablishment of continuity is usually possible. There appears to be no contraindication to removing more than the involved segment of bowel. This should place the point of anastomosis in more favorable territory. It would tend to reduce the number of residual diverticula and perhaps the statistical chance of recurrence. In this connection, it appears desirable to guard against delay at the anastomosis.

(7) It is suggested that a preliminary transverse colostomy be performed in all cases in which resection is contemplated, and that the period of delay before resection be from three to six months.

(8) If resection should for some reason be performed in the acute stage, an exteriorizing procedure, of the Mikulicz type, should be employed. It must be stated, however, that this technic could not be used in over one-third of our cases. Resection should be avoided in the acute stage of the disease.

(9) It is impossible to differentiate between carcinoma and diverticulitis in a few cases. In these, resection is indicated.

(10) Resection of the involved segment of the bowel appears to offer patients suffering from the more severe and complicated forms of diverticulitis the greatest hope for improvement. If carefully planned, the mortality should be low, serious complications few, and unsatisfactory late results infrequent.

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DISCUSSION—DR HENRY W CAVE (New York) The first cases of perforated diverticulitis with abscess formation in the American literature were reported by Dr George Emerson Brewer, an attending surgeon at the Roosevelt Hospital, before the American Surgical Association, in May, 1907 (35 years ago) He reported six cases

To some of us, certain suggestions offered by Doctor Smithwick in the surgical management of diverticulitis seem, at first, radical and they are radical when compared with our former notions of colon surgery But, assuredly, he has shown that the morbidity and the mortality can be lowered in properly selected and properly prepared patients No doubt, with the judicious use of the newer chemotherapeutic agents and methods of proximal decompression, the operative mortality can be still further reduced

In the past, most of us have treated the complications of the disease rather than attacking primarily the disease itself, this has necessitated emergency surgical measures Whereas, Doctor Smithwick has not stopped at that, but has gone on with elective procedures which promise a more effective and lasting cure

Cancer and diverticulitis are not infrequently seen coincidentally, but there is no evidence to assume that the presence of diverticulosis or diverticulitis predisposes to the development of a malignancy, this is accepted by all of us

The statement is accredited to the late Dr Daniel Jones, of Boston, that bleeding from the rectum is a prime symptom of malignancy and not diverticulitis Doctor Smithwick has stated that a history of bleeding is present in 15.7 per cent of patients known to have diverticulitis It is the experience of most of us that patients with the history of rectal bleeding sent to the roentgenologist for a barium enema, return with a report of diverticulosis or diverticulitis and not cancer

In eight, or 24.2 per cent, of the 33 cases resected by Doctor Smithwick the history, the roentgenographic findings, and the operative findings, all suggested malignancy, and there was no other way except resection to answer the problem usually the involvement is beyond the reach of the sigmoidoscope and the tell-tale biopsy specimen

From 1920 to 1942, a 21-year period at the Roosevelt Hospital, 43 patients of a group of 116 admitted to the Surgical Service were operated upon for acute or chronic diverticulitis of these, 11, or 25.6 per cent, were explored for a possible or probable malignancy These figures on this particular point in the two series the one from the M G H the other from the Roosevelt Hospital, are almost identical

In other respects our series correspond similarly to those of Doctor Smithwick, as to the indications for surgery, the methods of approach, and the mortality, except that in no instance have we resected the sigmoid for recurrent attacks of diverticulitis *per se*

Doctor Smithwick has resected the sigmoid in 33 individuals, with a relatively low mortality rate of 17.1 per cent, considering the nature of the disease And, in a group of 12 of 33 resected, he had a surprisingly low mortality of 6.1 per cent

To me, this group of 12, resected because of recurrent attacks of diverticulitis, is one of the principal features of his splendid presentation

Preliminary proximal colostomy he considers preferable to cecostomy and should be done in all cases where resection of the sigmoid is to be carried out. The wider the excision the lower the chance of leakage at the suture line and added security by suturing healthy bowel wall.

Wisely has he set a time interval of from three to six months of proximal decompression, by colostomy before proceeding with the resection.

Stenosis as a complication at the site of removal is not infrequent by the Mikulicz method in our own series.

In dealing with an inflammatory and not a malignant lesion I believe it can be stated with fairness that any type of exteriorization procedure is as complete and, to me, is safer than suturing the colon end-to-end or even side-to-side and I say this even in spite of the sulfonamide drugs and the Devine method of dysfunctioning the left colon.

In the series here presented colostomies were closed in 36 instances and only 52.8 per cent remained well indicating that the inflammatory lesion persisted. The late results following resection have proven more satisfactory.

Doctor Smithwick I am sure has stimulated us in an attempt to completely eradicate the diseased segment of the colon thus permitting these individuals to be well and not semi-invalids.

DR RICHARD B CATTELL (Boston Mass.) Doctor Smithwick's presentation of the difficulties of diverticulitis is of unique interest since there are 64 patients treated by every possible method of treatment that could be applied to diverticulitis and they are an unselected group. I think he has demonstrated very conclusively that a reasonable mortality can be expected if we delay resection to be a late and elective procedure.

Doctor Walker and I have recently reviewed our patients who have been operated upon for diverticulitis at the Lahey Clinic. We think there are only two operative indications, one the complications of inflammation and second and most important the indication of obstruction.

I would like to propose a relatively different conception with regard to the treatment of abscess in diverticulitis. From our experience and from that in the literature where free pus is drained into the peritoneal cavity the mortality has been high. I believe that if we delay operation in those cases with abscess until they either point in the left lower quadrant or by rectum and if operation is indicated do not operate in the field where the diverticulum is located but establish a colostomy of the transverse colon, we will reduce the mortality. Furthermore these abscesses frequently drain spontaneously into the lumen of the bowel.

We have because of our own mistakes and high mortality made another rule very clearly brought out by Doctor Smithwick and that is that with diverticulitis we do not perform a primary resection at any time if we know with what we are dealing. Where we have resected the diverticulitis as a primary procedure with a mistaken diagnosis of carcinoma our mortality has been 50 per cent. With regard to procedure of colostomy in the transverse colon if a long spur is formed greater ease will be experienced in the subsequent extraperitoneal closure.

DR CARL EGGERS (New York) I rise to discuss Doctor Smithwick's paper largely to call attention to the importance of the subject of diverticulitis and the danger associated therewith. In my own personal experience the condition has not been uncommon. I have seen 82 cases with acute diverticulitis of sufficient severity to warrant a surgical consultation. In 36 or 43.9 per cent a condition developed which required surgical intervention. In other words 36 patients were operated upon either for perforation or obstruction or mistaken diagnosis. Of those operated cases 20 or 24.4 per cent had perforation. Twenty-four per cent of the acute diverticulitis cases had perforation. Their operation was forced on the surgeon. That is what I want to call attention to. That was the group we had to handle surgically. Of that group ten died a mortality of 50 per cent.

The total mortality in the 34 cases operated upon was 23.5 per cent, which is restricted entirely to acute perforations. Among this group there were five patients with cancer, all of whom eventually succumbed to their disease.

DIVERTICULITIS OF SIGMOID

Of the late complications which follow this condition, one of the most annoying is the persistent fistulae. If the fistulae discharge only suppurative material, the patients do not mind so much, and some prefer to have the fistula drain itself rather than be subject to operation, but if there are feces draining, there is a different condition. During the last four or five years we have had four such cases. One preferred to drain and finally healed after about four years. Two were operated upon, and by complete excision of the fistulae and closing the sigmoid opening, it was possible to heal them. The fourth one has had several attempts at closure but it was not permanent.

Another interesting complication is sigmoid-bladder fistulae. I think much depends on the extent of the involvement in that and/or the place of attachment. If the place of attachment is close, the closure should not present much difficulty, if one uses prompt cleansing of the bowel and bladder both, and interposes a layer of omentum between the two sutures after completion. But the important thing is the danger of perforation. If the perforation can be avoided in some of the patients who have repeated attacks of pain and obstruction an operation of choice in those patients may be indicated, as Doctor Smithwick has stressed and there one can prepare them adequately the way one does in carcinoma. One of the difficulties with resection, however, in these cases is the length of involvement of the bowel. That is one of the very important differential diagnostic points. Carcinoma usually involves a small segment, diverticulitis, a long segment, so long you have to operate in diseased tissue if you want to resect the whole area. That is one of the very serious difficulties. Also, resection does not guarantee that one will not have recurrence. I have had two patients who had resection done, who later had recurrences, and one of them is under observation now. It was resected ten years and he was pretty well. Now he has recurrent attacks of severe pain resembling obstruction, and roentgenograms show very extensive diverticulitis along the whole sigmoid region.

DR CHARLES C LUND (Boston, Mass.) In connection with Doctor Smithwick's paper and Doctor Cave's comments on it both mention the occasional incidence of bleeding in diverticulitis. I want to call attention to the fact that that bleeding may be quite severe.

A few months ago a patient at the City Hospital, in Boston, came in with a history of a marked hemorrhage of fresh blood. He was in such shape that the interns transfused him as soon as possible after admission. During the time that the first transfusion was running into his veins, he called for the bed-pan, and a measured amount of 1500 cc of pure blood was evacuated. Transfusions were repeated. Many pints of blood were given. We got far enough ahead of the hemorrhage so that, on the second morning, it seemed reasonable to try a desperate operation. The situation that was found was a fistula that had burrowed from a diverticulum into the ileac fossa. I did not feel justified, with the scarred conditions found, to try to do anastomosis. I tied off the artery; the patient did very well for a few hours, and then died of hyperpyrexia, which possibly is accounted for by the period of pretty severe shock or low blood pressure, that he was in before the operation. I do not know, I think that is a unique case.

Doctor Berring and I have studied it to some extent. We find no reference to such an instance in either surgical or pathological literature. If any of you have had any experience approximating that, I would appreciate it if you would speak to me about it.

I think Doctor Smithwick's paper was really very, very valuable. In our experience, which has not been studied at the City Hospital, I would say it is my personal impression that when our cases have done well they have been handled in the way in which Doctor Smithwick's cases have been handled. When they have not done well they have been handled in the way the cases at the General that have not done well have been handled, as he has shown.

DR R H SMITHWICK (closing) I think the discussion this afternoon in regard to diverticulitis is fairly representative of what you find in the literature namely, that there is considerable difference of opinion about what should be done and when it should be done. Strangely enough although there is a great deal of literature on certain aspects of this problem there are surprisingly few reports of late results of any maneuver whatsoever. Many people, of course, have been operated upon, but there are very few late results in the literature for which reason it is difficult for one to make a decision as to what really should be done under various circumstances. My impression is that there is a real need for further reports of late results of various forms of treatment.

SURGICAL TREATMENT OF MALIGNANT LESIONS OF THE SIGMOID—WITH EXTENSION^{*}

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THE OPERABILITY of malignant lesions of the sigmoid is limited by the presence of distant metastases or the extensive involvement of adjacent structures, removal of which would jeopardize life. The necessity for resecting areas of small bowel, uterus, tubes and ovaries with the sigmoid has been met successfully and is not regarded as being particularly dangerous. When, however, the tumor invades the urinary bladder—especially if the invasion is extensive or happens to be near the trigone—operation has been approached in a spirit of defeatism even though the lesion be otherwise operable. Accordingly, many cases of carcinoma of the sigmoid are denied radical operation because the operator fears that resection of part of the urinary bladder with the bowel is too hazardous.

Little mention is made of this extension and its treatment in the literature covering the subject. In a few instances authors either condemn the technical gymnastics required or state simply that if the bladder involvement is small, entrance into that organ should not be feared if it is necessary to complete a radical resection. Yet it seems surprising that with what is known of partial or complete cystectomy for other conditions we should not encounter more reports of experience with the partial removal of the urinary bladder in cases of carcinoma of the sigmoid with extension. The purpose of this communication is to compare the results in two cases of carcinoma of the sigmoid with involvement of the urinary bladder in which we accepted the idea of palliation solely because of the urinary bladder involvement with those in four others in which resection of the diseased portions of the bladder was carried out.

CASE REPORTS

Case 1—N Y H No 274152 W P, male, age 60, had complained of increasing constipation over a period of one year. Two months before admission the stools became narrow and abdominal cramps developed which were relieved by the passage of stools or flatus. There were no bloody stools. He had nocturia three to four times for the past two months, and had lost 60 pounds since the onset of his symptoms. The positive physical findings included evidence of weight loss, arteriosclerosis, complete edentia, and a palpable, fixed mass in the suprapubic region. Digital examination of the rectum was negative. Proctoscopic examination revealed a fungating lesion at 16 cm that proved to be adenocarcinoma on microscopic examination. All laboratory tests were negative with the exception of occult blood found on stool examination. Exploratory celiotomy revealed a large tumor of the sigmoid invading the fundus and posterior wall of the bladder, no liver or distant lymph node metastases were noted. The lesion was considered inoperable, and a right transverse colostomy was performed. The patient is living, with little change in his condition, one year and two months following operation.

^{*} Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

Discussion Resection in this case would have required the removal of two-thirds of the bladder with the sigmoid by the abdominoperineal method. The radical operation should have been attempted.

Case 2—N Y H No 282163 E C, male, age 60, was admitted to the Urological Service, with the complaint of weight loss, watery diarrhea and later constipation for a period of one year. Six to seven months previously there developed tenesmus, urinary frequency and burning on urination. Two months before admission the patient observed the passage of gas from the urethra. These symptoms became progressively worse and weakness became pronounced. Examination revealed emaciation, a mass in the left lower quadrant and suprapubic region and an enlarged prostate. All laboratory examinations were negative except for the stools which were positive for blood. Pyelography revealed left hydronephrosis and left hydroureter. Cystoscopic examination revealed a large defect in the fundus of the bladder, due presumably to carcinoma of this organ. Barium enema showed an irregularity in the sigmoid, and on proctoscopic examination a lesion was seen at 15 cm which proved to be adenocarcinoma. A transverse colostomy, without exploration, was performed under local anesthesia. Postoperatively, feces and gas continued to pass per urethra. Severe lower abdominal pain developed on the ninth post-

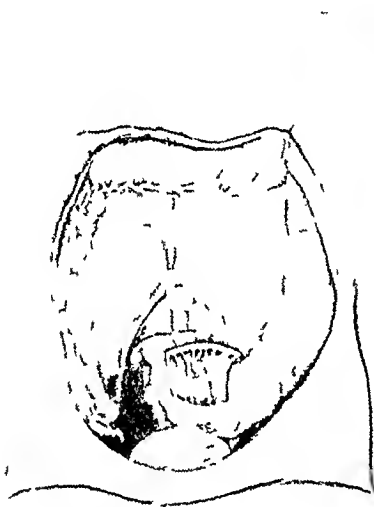


FIG 1—Case 3 Extension of carcinoma into the fundus of the bladder



FIG 2—Case 3 Repair of bowel and bladder at end of operation

operative day, with signs of peritonitis from which he died on the next day. Postmortem examination revealed carcinoma of the sigmoid infiltrating the fundus of the bladder, resulting in rectovesical fistula, extravescical abscess with perforation and generalized peritonitis.

Discussion The transverse colostomy was established as a preliminary step to radical resection, and the postmortem findings confirmed the suspicion that the growth could have been removed if infection had not terminated the patient's life.

Disappointed by the poor results of such palliative procedures, we have been led to perform much more extensive operations in the following four cases including, when necessary, wide resection of the bladder.

Case 3—N Y H No 199533 L B, female, age 65, had noticed increasing constipation for three months, with ribbon stools for one month, and occasional abdominal cramps. No bloody stools were noted, and there was no weight loss. Physical examination showed moderate arteriosclerosis but was otherwise negative. Stools were negative for blood. Barium enema showed constriction of the sigmoid. Proctoscopy was negative.

Procedure Exploration revealed that there was a large tumor of the sigmoid fixed to the fundus of the bladder but that actual invasion of the bladder was not extensive. A portion of the fundus was excised with the bowel tumor, thus freeing the intestinal mass. This was resected radically and end-to-end anastomosis performed. The resultant opening in the fundus of the bladder was sutured with catgut and silk, and a cecostomy was performed. The abdominal wound was closed with catgut and silver wire retention sutures and a retention catheter was inserted per urethra.

Course The abdominal wound became infected but responded to simple drainage. The urinary catheter was removed on the eleventh postoperative day. Normal bowel movements occurred on the twenty-sixth day.

Follow-Up There is no sign of recurrence three years and ten months postoperatively.

Case 4—N Y H No 274729 A B, male, age 66, had complained of passage of gas per urethra for a period of two months, urinary frequency, burning, and failure to empty the urinary bladder completely when voiding. Bowels were regular but the stools con-

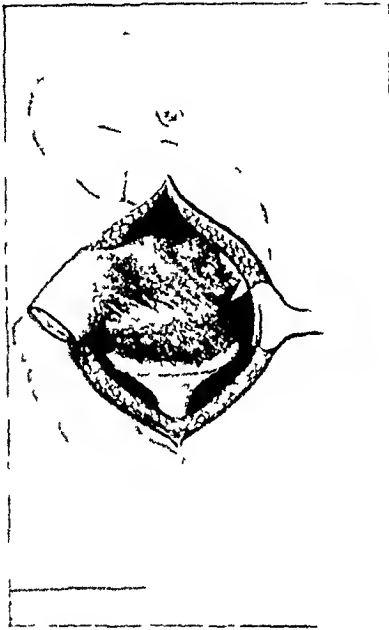


FIG 3—Case 4 Extensive involvement of upper half of urinary bladder

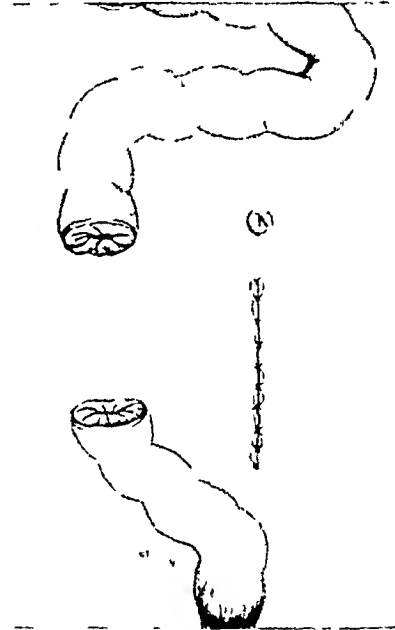


FIG 4—Case 4 Remaining bowel segments, later anastomosed end to end

tained pink, jelly-like material at times. He had a poor appetite due to the fact that eating made all the symptoms worse, and had lost 25 pounds in weight.

Physical Examination showed obesity and moderate arteriosclerosis. There was a hard suprapubic mass, about the size of a grapefruit which was slightly tender. The prostate was moderately enlarged. Laboratory tests showed 3+ albumin and numerous W B C and R B C in the urine. All stools were positive for blood. Proctoscopic examination was negative. Barium enema showed a lesion of the sigmoid resembling diverticulitis.

Preoperative Course The patient was placed on clear liquid diet, with definite improvement. A second barium enema showed no change from the first. Soft diet was instituted at this time, with a return of the symptoms, and the passage of feces in the urine as well as more gas per urethra was now noticed.

Procedure Because of his failure to improve, transverse colostomy was attempted under local anesthesia. A greatly redundant sigmoid, which was encountered in the wound, necessitated using the portion of that organ proximal to the lesion for the colostomy instead of the transverse colon. Following this, the patient improved con-

siderably, the passage of gas and feces per urethra being markedly decreased. His course following the colostomy was complicated by a pulmonary embolus, but recovery was prompt. Thirty-eight days after the colostomy, under open drop-ether anesthesia, a left rectus incision was made, and the huge lesion in the sigmoid was found to involve the upper half of the urinary bladder. On first inspection, complete fixation of the mass with a considerable amount of infection was noted. However, there were no distant metastases, and an attempt was, therefore, made to free the mass. The peritoneum covering the bladder was incised together with the peritoneum lateral to the sigmoid. This allowed a line of cleavage which resulted in the mobilization of the bladder with the intestinal tumor. Further examination of the large mass revealed that if radical removal were to be carried out it would necessitate the excision of two-thirds of the bladder. At the proper site, just above the trigone, the bladder wall was incised, and by carrying the incision completely around the bladder the entire mass was mobilized enough to allow it to be raised outside the abdominal cavity. Kocher clamps were placed on the bowel at suitable distances below the lesion, and by dividing between the clamps the mass was further delivered, so that the mesentery beneath the tumor could be clamped and resected. After removing the proximal bowel to the level of the colostomy, the resection was completed.

At this point, however, the patient was in moderate shock and, although an anastomosis would have been possible, it was deemed wiser to leave the colostomy opening undisturbed and bring the distal segment out through the lower right rectus region. After securing proper hemostasis of the mesentery and bladder wall, the circular bladder edge was sutured around the end of a mushroom catheter, which was then brought out through the lower end of the left rectal wound as a cystostomy tube. Several cigarette drains were placed in the rectovesical pouch and the celiotomy wound closed with through-and-through silver wires. Shock was readily counteracted by the ordinary methods.

Pathologic Examination revealed adenocarcinoma of the sigmoid with extension into the urinary bladder, metastases to the regional lymph nodes, markedly inflamed and necrotic bladder wall, and a small polyp in the sigmoid.

Course Unremarkable until the tenth postoperative day. The cystostomy tube was removed and several hours later there was an alarming hemorrhage from the suprapubic wound as well as from the urethra. This ceased after half an hour, and, with the aid of transfusions, the patient's condition improved. A retention urethral catheter was inserted on the twentieth postoperative day. The wound healed rapidly, and following removal of the catheter on the forty-fifth postoperative day, the patient was able to void satisfactorily. He was discharged 66 days after the radical procedure. At this time the left rectus wound was completely healed and the right rectus region contained two colostomy openings—the upper one, being proximal, was the functioning colostomy.

Improvement was now quite rapid. The patient returned to work, but was considerably handicapped by the nuisance of the colostomy. Six months after the resection he was readmitted to the hospital, and after four days of preparation with sulfadiazine, irrigations and clear liquid diet, under open drop-ether anesthesia, the two colostomy openings were dissected free of the abdominal wall, the ends of both resected about two inches from the opening, and end-to-end anastomosis performed, without proximal decompression. Sulfadiazine was continued postoperatively, to include seven days in all. Passage of flatus was noted in 72 hours, the bowels moved normally on the fifth day, both wounds healed per primam, and he was discharged on the twentieth postoperative day.

Follow-Up The patient now weighs 220 pounds, and has normal functioning bowel and bladder behavior. There is a small incisional hernia in the left rectus wound. There is no sign of recurrence or metastases one and a half years following the resection.

Case 5—NYH No 297121 S Z, male age 51, complained of diarrhea, urgency, tenesmus and passage of foul-smelling mucoid material per rectum. A slight amount of blood was passed with the stools. There were intermittent abdominal cramps, urinary

frequency, cloudy urine, and the passage of flatus per urethra at times. There had been a loss of weight of 64 pounds.

Physical Examination showed emaciation, and a palpable, large, hard, fixed mass in the rectovesical pouch. Proctoscopy revealed a fungating mass at the level of 15 cm, proven to be adenocarcinoma microscopically. Laboratory tests showed 2+ albumin, and many W B C and R B C in the urine. R B C 25 million, W B C 21,000, stools positive for blood. Cystoscopy showed intrusion and invasion of the bladder wall by bowel malignancy.

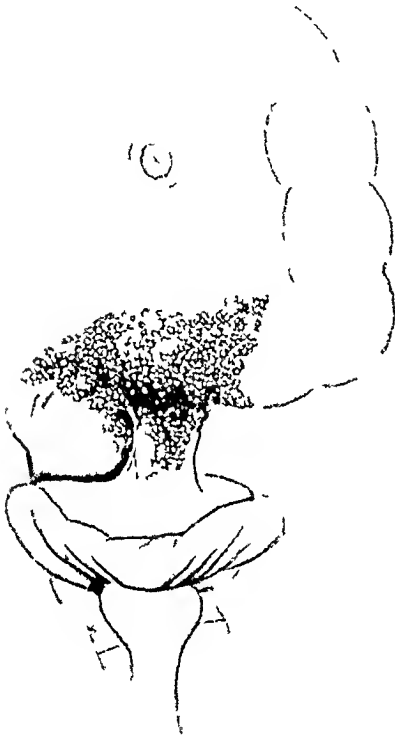


FIG 5—Case 5. Extension of carcinoma into posterior aspect of the bladder.

After securing hemostasis, this was closed with interrupted catgut sutures. The tumor was still fixed to the posterior peritoneal wall, and, after locating the right ureter which was obstructed by the tumor, the posterior peritoneum was incised and the mass finally freed sufficiently to be delivered into the wound. The section with the invaded bladder wall attached was now resected with adequate margin in the bowel and mesenteric areas. Because the lesion was situated low, it was impossible to make an anastomosis. The lower end of the bowel was, therefore, turned in and the proximal end was brought out the upper region of the wound. A tube was inserted in the fundus of the bladder and brought out the lower end of the wound. Several cigarette drains were placed in the rectovesical pouch, and the wound closed with through-and-through silver wire sutures.

Course Sulfadiazine was continued for a period of seven days. The suprapubic tube was removed on the tenth postoperative day, and on the twenty-fourth day the patient was voiding normally. His condition improved markedly, and there was immediate cessation of the urinary inflammatory symptoms. He was discharged 41 days after the resection, with the wound completely healed. The transverse colostomy is the functioning anus, and there is a mucous fistula present in the left rectus incision.

Procedure Transverse colostomy was performed under local anesthesia. After opening the colostomy the patient improved slightly, but began to run a septic course with high temperature and chills, due to marked urinary infection. This continued with a consequent downhill course until his condition became precarious. Several observers felt that because of the urinary infection, fixation of the mass, and obvious bladder invasion, resection would not only be dangerous but futile. However, after many transfusions and prophylactic administration of sulfadiazine, a midline incision was made under ether anesthesia. There were no metastases in the liver and no preaortic lymph nodes were involved. A greatly inflamed mass was located in the sigmoid, which was fixed to the posterior bladder wall. After incising the bladder peritoneum, the entire mass, with the bladder, was freed. The bladder involvement extended almost down to the trigone in a longitudinal manner. Incisions were made into the bladder, allowing margins on both sides. When the tumor was removed from the bladder there remained a long longitudinal incision in the posterior wall from the fundus to the region of the trigone. After securing hemostasis, this was closed with interrupted catgut sutures. The tumor was still fixed to the posterior peritoneal

CARCINOMA OF SIGMOID

Follow-Up Ten months postoperatively there is no recurrence and no evidence of metastases. He has gained weight and strength and is voiding normally.

Case 6—N Y H No 284479 J J, male, age 51, had noted malaise, chills, fever, and a dull pain over his lower abdomen for three weeks. There was marked urinary frequency, dysuria and cloudy urine. Constipation became more marked during the past two months. He had passed a single bloody stool one month before admission.

Physical Examination showed a pale, acutely ill man. Abdominal and rectal examinations were negative. Laboratory tests showed many W B C and R B C in the urine, R B C 3.3 million, W B C 32,000, stools negative for blood. Proctoscopy revealed no tumor, but what appeared to be urine could be seen dripping into the rectum. Cystoscopy showed a rectovesical fistula located just above the trigone. Barium enema revealed a lesion of the sigmoid suggestive of carcinoma.

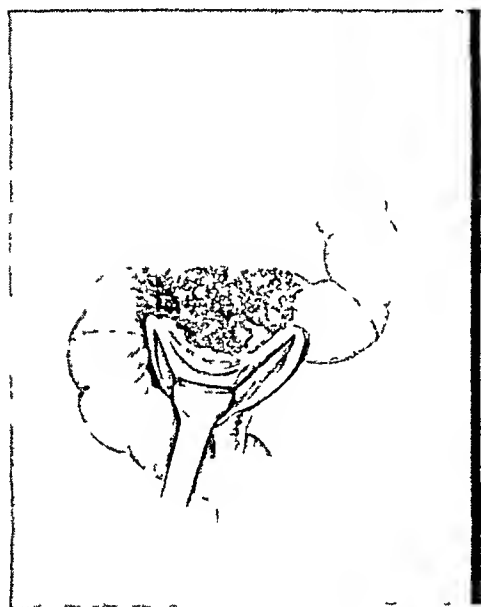


FIG 6—Case 6 Extensive involvement of posterior bladder wall



FIG 7—Case 6 Marked involvement of bladder present six months after first resection

Procedure A transverse colostomy was performed, which resulted in marked improvement in his general condition. Many blood transfusions were given and sulfadiazine was administered preparatory to resection, which was attempted through a left rectus incision, three weeks following the colostomy. No liver or distant lymph node metastases were noted. The tumor was located in the sigmoid, and extension was discovered into the bladder in one small area in the region of the trigone. There was a considerable amount of infection present. An incision was made into the bladder "coring-out" the fistulous tract, but this could not be accomplished with a large margin because the ureteral orifices were in close proximity to the invaded area, but because of so much infection it was hoped that the actual invasion would be minimal. The opening in the bladder was closed with catgut. It was now fairly simple to free the sigmoid, resect it with good margin, and perform an end-to-end anastomosis. Two cigarette drains were placed in the rectovesical pouch and the wound closed with catgut and silver wire retention sutures. A retention catheter was placed in the bladder per urethra.

Course An intra-abdominal abscess developed, which was drained three weeks postoperatively. Following this, improvement was marked and healing of the wound was rapid. Six weeks after the resection the transverse colostomy was closed, and the patient was discharged, with normal rectal and bladder function. He gained in weight and strength and remained well until six months following the resection. At this time he began to have hematuria, which was severe and continuous. Profound anemia and weakness followed. Cystoscopic examination at the time revealed the entire urinary bladder to be involved in an infected neoplastic process, biopsy of which proved it to be

adenocarcinoma originating from the rectum and showed the same morphologic structure as that seen in the sigmoid lesion. Roentgenotherapy offered no hope and nothing was planned therapeutically until the patient and his family insisted that anything be attempted which might offer even the slightest hope. Accordingly, bilateral ureterostomies were performed, following which the patient's condition improved rapidly. After several blood transfusions and sulfadiazine prophylactically, the left rectus wound was reopened and, again, no liver or distant lymph node metastases were noticed. There were a few small involved nodes in the mesentery beneath the anastomosis. The urinary bladder was enlarged and was obviously involved with tumor in its entirety. The bladder peritoneum was incised and the entire bladder freed by blunt dissection, continuing this dissection anteriorly under the symphysis and posteriorly so that both seminal vesicles and prostate gland were now clearly defined and freed. The posterior urethra was incised and vessels clamped, following which the bladder, prostate and seminal vesicles were removed *en bloc*. The sigmoid was again resected, leaving a small stump of rectum in the rectovesical pouch which was turned in by silk sutures. The proximal loop was brought out the upper end of the left rectus wound and cigarette drains were placed in the rectovesical pouch. The lower portions of the ureters were, of course, removed with the bladder. The patient withstood this procedure well. Some difficulty was encountered with the ureterostomies, but the patient improved to such an extent that he was up and about the ward. After several months of improvement, his condition began to decline and he died with palpable carcinoma in the rectal stump and obvious metastases in the liver, 13 months after the first resection, and six months after the radical resection of the bladder, prostate, seminal vesicles, ureters and sigmoid.

Discussion Because of the site of invasion which was in close proximity to the interureteral ridge, the bladder involvement was not given a proper margin in the first operation. The second radical resection was, in reality, experimental, but might have offered the patient a slight chance of recovery. It is obvious from the course that had the second radical procedure been carried out originally, a better result may have been anticipated.

SUMMARY

It should be pointed out that a redundant sigmoid colon is one which attaches itself to the bladder and, therefore, allows extension of its tumor into the bladder. If no redundancy is present, the sigmoid usually lies against the posterior abdominal and pelvic walls, which position reduces the possibility of extension. The redundancy, however, is an asset if resection is to be performed.

The use of preliminary colostomy and prophylactic sulfonamide therapy, as well as the other better known preoperative agents, is recognized in the preparation of these patients for operation.

These cases are presented as evidence supporting radical operations in malignant disease of the sigmoid with extension into the urinary bladder. It is suggested that neoplastic involvement of the bladder is no reason, in itself, to withhold the radical operation. Partial resection of the urinary bladder may be accomplished without significant danger to the patient or resultant malfunction of the genito-urinary system. The operation of total cystectomy, seminal vesiculectomy and prostatectomy, combined with resection of the sigmoid neoplasm *en bloc*—if that is necessary to offer cure—is demonstrated to be possible.

Whether or not the patient with bilateral ureterostomies and permanent

colostomy is one whose life in such a state is a fair exchange for death from carcinoma of these organs cannot be decided with accuracy until many similar cases and their experiences are recorded

DISCUSSION—DR VERNON C DAVID (Chicago) Doctor Bowers has brought to our attention a very important viewpoint in the treatment of malignant lesions of the large bowel, in that he advocates in this radioresistant group of tumors an extension of the indications for radical removal. The principles underlying this extension of indications for radical surgery must include a reasonable mortality rate and long-term survival rate as well as reasonable assurance that the growth and its extensions are completely removed.

I have been asked to discuss this paper because Doctor Gilchrist and I have recently reviewed our experience during a ten year period, of 179 radical operations for cancer of the rectum, where there were 74 favorable cases, with no question of operability, and another group of 105 patients having one or more doubtful factors which clouded operability (Table I)

TABLE I

CAUSES OF QUESTIONABLE OPERABILITY IN 105 PATIENTS

Over 65 years of age	38
One or two nodules in the liver	15
Adiposity	10
Obliterative pelvic peritonitis	9
Resection of prostate or urethra with the rectum	7
Resection of rectovaginal septum with the rectum	6
Peritoneal plaques over the tumor	5
Diabetes	5
Removal of all or part of uterus or adnexa	4
Adherent to prostate (removal of capsule)	4
Adherent to bladder	4
Adherent to rectovaginal septum	6
Adherent to sacrum	4
Adherent to uterus	1
Resection of another loop of bowel	1
Marked coronary disease	2
Pregnancy	2
Removal of local recurrence	3
Fixed to abdominal wall	2
Asthma and bronchiectasis	1
Involvement of inguinal nodes	2
Double carcinoma of the rectum	1
Involvement of rectal fistula by adenocarcinoma of the rectum	1
	<hr/>
	133

In the favorable group the hospital mortality was 4.3 per cent, and in the doubtful factor group it was 9.5 per cent.

In the group where the indications for operation were liberal there were 38 patients over 65 years of age with a mortality of four, or 10.5 per cent (Table II)

TABLE II

AGE AND RADICAL OPERATION FOR CANCER OF THE RECTUM

18 patients between 65-70 years	1 death—embolism
12 patients between 70-75 years	1 death—embolism
4 patients between 75-80 years	1 death—pneumonia
4 patients between 80-85 years	1 death—pneumonia
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38 patients over 65 years	4 deaths—10.6%

Where the tumor was adherent to structures outside of the bowel we resected part of the prostate in 11, the rectovaginal septum in six, the dome or posterior half of the bladder in one, a part of the base of the bladder in five, the uterus or adnexa in five, the ureter in two, the urethra in one and another loop of bowel in one. In this group of patients there were three postoperative deaths. In four other patients with carcinoma

of the sigmoid we resected the dome or posterior half of the bladder, with one death. Time does not permit details of long term survival but I can say that while there will be a higher percentage of local recurrence in this group than in a favorable group, there will also be many patients who live three to five years after the operation.

We have not been impressed with the soundness of undertaking radical operations where definite liver involvement is present. However, there are patients having one or two doubtful nodules in the liver at the time of operation where the differential diagnosis between cancer and adenoma or lymphangioma of the liver is difficult to make. We believe it proper to carry out the radical operation in such patients. Of 16 such instances four have died of cancer of the liver on an average of ten months following operation. Four are alive three to five years postoperatively.

Adiposity, obliterative peritonitis, lymph node enlargement, circumscribed perforation of the tumor or fixation to the abdominal wall have not been considered as contraindications to radical removal of the tumor. In carcinoma of the sigmoid, descending colon and cecum, with fixation to the abdominal wall, wide removal of the abdominal wall with the tumor has resulted in several five-year cures.

Until surgery is supplanted by a better method of treatment in cancer of the bowel we believe that the indications for radical surgery should be broadened for even though the mortality rate will be higher and recurrences more frequent, a larger number of patients will be given the chance of a long term cure.

DR RICHARD K. GILCHRIST (Chicago). On examining specimens of carcinoma of the sigmoid which required resection of viscera firmly adherent to them we have been surprised to see how often this fixation is due to inflammation and not to extension of the tumor.

This slide shows the resected specimen of carcinoma of the sigmoid with resection of a full-thickness of the bladder. The large marker leads into an abscess cavity between sigmoid and bladder. The three smaller markers serve to identify diverticula above the tumor.

The second slide shows this same specimen from the other side. Sections through the wall of the bladder fail to show carcinomatous invasion; the fixation was by inflammation. It is interesting to note that the three diverticula are in line with the point of fixation around the abscess.

This second patient had a large carcinoma and the resected specimen of the sigmoid and full-thickness of the bladder is shown. There are three fistulae into the bladder; each of these showed carcinomatous infiltration.

Of five specimens where the full-thickness of the bladder was resected with the carcinoma of the sigmoid, one had carcinomatous infiltration; in three the fixation was by firm inflammatory adhesions and one specimen was lost and the original sections were not taken through the adherent area. Interestingly enough, among nine other specimens of carcinoma of the sigmoid firmly adherent to other loops of bowel, uterus or abdominal wall, the fixation was due to inflammation in seven and infiltration in two.

It seems to me that we are apt to lose sight of the fact that the sigmoid may have become firmly adherent to the bladder or other viscera as a result of previous diverticulitis. Carcinoma is then superimposed upon this. With obstruction and the accompanying inflammation, it is impossible to tell the extent of the carcinoma. Of course, the inflammatory fixation may be due to slight perforation of the tumor and infection about this. These findings have led us to the conclusion that in carcinoma of the sigmoid the local mass outside of the bowel is very apt to be due to inflammation. This inflammation either arises from diverticula or results from inflammatory perforation of large obstructing tumors. Many of these can be successfully resected with a fair chance of permanent cure. One precaution must be taken. When the tumor is firmly adherent to another structure there is often an abscess between the two. Therefore we do not separate firmly adherent structures but attempt to resect a sufficient layer of the structure adherent to the sigmoid so that the abscess is not opened.

DR RICHARD B. CATTELL (Boston). Doctor Bowers has taken a step that I think is very laudable in extending operative indications to a very marked extent. Doctor Sugarmaker and I have just reported this month on our cases from 1939 through 1941. Eighty-six per cent of all patients during that period with carcinoma of the bowel had

a resection Twenty per cent of all of those cases had invasion of some organ, either bladder, small intestine, or other organs Ten per cent of them had liver metastases and during this period we have resected the secondary metastasis in the liver in three cases I think that until we have tried extensive resection in malignancy much more than we have at present, we should continue with such efforts as Doctor Bowers has made

DR RALPH F BOWERS (closing) I want to thank Doctor David and Doctor Cattell for expressing an opinion about these radical procedures

Doctor Gilchrist made a point that I believe got us into trouble in the last case It is almost impossible, with the extensive infection that is present, to tell which is infection and which is tumor Our experience with the first three cases has shown that the invasion of the bladder was not as marked as we thought But we were able, by reason of that fear, to give the involved portion of the bladder a very good margin In the last case, because extension was in the region of the trigon, we believed that infection would be present to a greater extent than tumor therefore, the coring-out, and, subsequently, the recurrence

I did not make the point clear but I think that in the last case had we undertaken the radical procedure, with the first part of the operation, we might have offered now a permanent cure



LONG REMEMBER

In the Civil War nothing was known of "germs" Bacteriology was an unknown science

'It can be understood' wrote Dr William W Keen "why we surgeons in 1861-65 utterly unaware of bacteria and their dangers, in our ignorant innocence committed grievous mistakes which nearly always imperilled life and often actually caused death May *le bon Dieu* forgive us our sins of ignorance We operated in our old blood-stained and often pus-stained coats, the veterans of a hundred fights We operated with clean hands in a social sense, but they were undisinfected hands To the surgeon the spotless hands of a bride are dirty We used undisinfected instruments from undisinfected plush cases, and still worse, used marine sponges which had been used in prior pus cases and had been only wished in tap water If a sponge or an instrument fell on the floor it was washed and squeezed in a basin of tap water and used as if it were clean

"Our silk to tie blood vessels was undisinfected One end was left long hanging out of the wound and after three or four days was duly pulled upon to see if the loop on the blood vessel had rotted loose When it came away, if a blood clot had formed and closed the blood vessel, well and good, if no such clot had formed then a dangerous 'secondary' hemorrhage followed and not seldom was fatal The silk with which we sewed up all our wounds was undisinfected If there was any difficulty in threading the needle we moistened it with (as we now know) bacteria-laden saliva, and rolled it between bacteria-infected fingers We dressed the wounds with clean but undisinfected sheets shirts, tablecloths, or other old, soft linen rescued from the family rag bag We had no sterilized gauze dressings, no gauze sponges"

—Ciba Symposia

THE MECHANISM OF ACTION OF ROENTGENOTHERAPY UPON INFECTION*

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AMONG both surgeons and roentgenotherapists there is much difference of opinion regarding the value of roentgen ray irradiation in the treatment of acute infections. This may be attributable, at least in part, to the fact that it is difficult and often impossible to evaluate, by clinical means alone, the merit of a therapeutic agent which has an effect short of a specific one. Such an evaluation is possible only by means of controlled comparative studies in volume, circumstances attainable only in animal experiments. A report of an investigation of this kind follows.

Experiments—The original problem was designed to determine the effect of the sulfonamide drugs as well as roentgen ray irradiation upon peritonitis. But, as the investigation progressed, certain unanticipated findings appeared and altered the direction of study. Since the intraperitoneal route of bacterial inoculation was used in the original experiments it was continued throughout, to provide a consistent basis for comparison. For the inoculations a pathogenic culture of hemolytic *E coli* was used. This culture was obtained from the Agricultural College, where it had been isolated from calves afflicted with a severe epidemic type of dysentery. Its minimal lethal dose for rabbits was established at two slants of 48-hour growth.

The micro-organisms from the slants were injected into the peritoneal cavity suspended in a standard solution of gastric mucin. In each series of experiments several animals were inoculated at the same time and, to be more certain that each animal received an equal number of micro-organisms, the slants were pooled, and from the pool each animal received 20 cc of the mucin suspension, which in each instance provided the minimal lethal dose of bacteria. One and usually two or more recipients of each pool were reserved as control animals to verify, constantly, the virulence of the culture. On three occasions a control survived, and in each series represented by these controls all observations were discarded as invalid and the investigation halted until the original virulence of the culture had been restored by passage through animals.

The only criterion by which the effectiveness of the therapeutic agent was judged was survival and, to a lesser extent, the duration of survival. No records of temperature or other physical evidence of infection and toxemia were obtained.

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

In several animals the evolution of the peritoneal exudate was followed. At frequent intervals after inoculation, exudate was aspirated and the bacteria and leukocytes in ten representative fields were counted and an average value calculated. But as it became apparent that these studies made no contribution to the problem at hand they were discontinued as a routine procedure. For the same reason this data is omitted from this report except for the two illustrative records (Table I).

TABLE I

REPRESENTATIVE PERITONEAL EXUDATES OF RABBITS AFTER INTRAPERITONEAL INOCULATION WITH A CULTURE OF HEMOLYTIC *E. coli* IN 20 CC OF GASTRIC MUCIN

Rabbit No *	Inoculated Time of Smear	Progress	Bacteria	Polys	Phagocytes	Monos
10	4-4-40 3 P M	1 slant	about 36,000 M			
	4-4-40 6 P M	Very ill	Packed	55	Occasional	2
	4-5-40 7 A M	Very ill	Approx 100	80	2	1
	4-5-40, 2 P M	Improved	82	78	10	3
	4-6-40, 2 A M	Much improved	Scattered in clumps	48	7	5
	4-8-40 5 P M	Well	Occasional	10	8	8
	4-4-40 3 P M	2 slants	about 72,000 M			
	4-4-40 6 P M	Very ill	Packed	21	0	4
14	4-4-40 8 P M	Moribund	Packed	12	3	1
	4-4-40 10 P M	Dead				

* Both rabbits are from series used to establish a constant minimal lethal dose. Rabbit No. 10 received a sublethal dose.

Postmortem examinations were made on all animals, but since there was no consistent or significant difference in the findings within the peritoneal cavity individual reports are omitted. In no instance was there a picture of peritonitis as observed in man. There was always an increased amount of peritoneal fluid varying from 5 to 30 cc. It was slightly to moderately turbid and usually blood-tinged but never thick and grossly purulent. The peritoneal surfaces were only slightly to moderately injected but, in common with the omentum, usually contained a few to numerous punctate areas of hemorrhage. There was definitely more injection of the peritoneal surfaces of the irradiated animals. The bowel was distended. Fibrin was singularly absent. The pleural cavities usually contained a small amount of clear fluid.

In five animals blood cultures were taken immediately following inoculation and every 15 minutes for one hour. All cultures were sterile.

In establishing the minimal lethal dose of the culture it was found that the quantity necessary consistently to cause death did so within 12 hours. Some of the animals which survived longer than 12 hours when a lesser dose was given, recovered. Therefore, the larger or consistently fatal doses were used throughout the experiments.

The Effect of Sulfanilamide and Sulfathiazole—In eight rabbits the abdomen was opened under local infiltration anesthesia. In each of six, one Gm of sulfanilamide powder was spread widely over the peritoneal cavity, and in two of these the abdomen was simply closed. In the remaining four, the

wounds were closed around small catheters through which the peritoneum was inoculated and then the catheters removed. This procedure assured retention of all the injected fluid. Two animals served as controls and received only inoculations given through catheters.

The two controls died in six and 11 hours, the four sulfanilamidized and inoculated rabbits died in four, five, eight and ten hours. The two which received only sulfanilamide survived and despite the fact that they received enormous doses, at no time did they show evidence of drug intoxication.

An identical series of studies with sulfathiazole gave essentially the same results, except that one of the two rabbits which received only sulfathiazole died on the third day, with postmortem findings of patchy consolidation of both lungs.

In a third series, seven rabbits were given the culture intraperitoneally. Two served as controls and died in five and one-half and seven hours. One hour before inoculation each of the remaining five were given 50 cc of 0.8 per cent solution of sulfanilamide subcutaneously. They died four, five, five, six, and eight hours after inoculation.

In a fourth series, four rabbits were given the culture and 1 Gm of sulfanilamide intraperitoneally and one, a control, was given the culture only. This series differed from the others in that the peritoneal cavity was not opened. The sulfanilamide powder along with the bacteria was suspended in the solution of mucin and deposited in the peritoneal cavity through a needle. All animals died. The periods of survival were five, ten, 14, and 14 hours. The control lived ten hours.

Not only did the use of sulfanilamide and sulfathiazole powder, as topical applications, and as subcutaneous injections, fail to prevent death of these animals, but it actually decreased the duration of survival.

Roentgenotherapy—All animals received irradiation according to a fixed formula. It was given through one anterior port over the entire abdomen, with the remainder of the body shielded with lead. It was delivered through an inherent filter of 3 Mm aluminum and an added filter of 0.5 Mm copper and 1 Mm aluminum at 50 cm target skin distance, activated by 140 kilovolt constant potential, and 15 milliamperes. The intensity of the beam was 20 r per minute, measured in air. The dosage was determined by the duration of exposure and was varied accordingly.

Postinoculation Irradiation—Ten rabbits were inoculated with two slants in 20 cc of mucin. Two served as controls, and eight received 1000 r irradiation immediately after inoculation. Of these two received a single dose of 100 r, and two, a single dose of 200 r within 20 minutes after inoculation. They survived only five hours.

Four received 20 r every two hours until they died five, six, six, and seven hours after inoculation. Both controls died in five hours. A possible cause of failure of roentgen ray irradiation to alter the course of events resulting from the inoculation in this series of animals is suggested in the results of the subsequent experiments.

Premoculation Irradiation—The rabbits in this series received roentgen ray irradiation at periods prior to inoculation varying from 16 weeks to 24 hours. In all, there were eight different intervals of time between irradiation and inoculation, and because the experimental procedure was not constant this series is reported under eight headings

PERCENTAGE OF SURVIVORS AFTER INOCULATION AND X RAY THERAPY

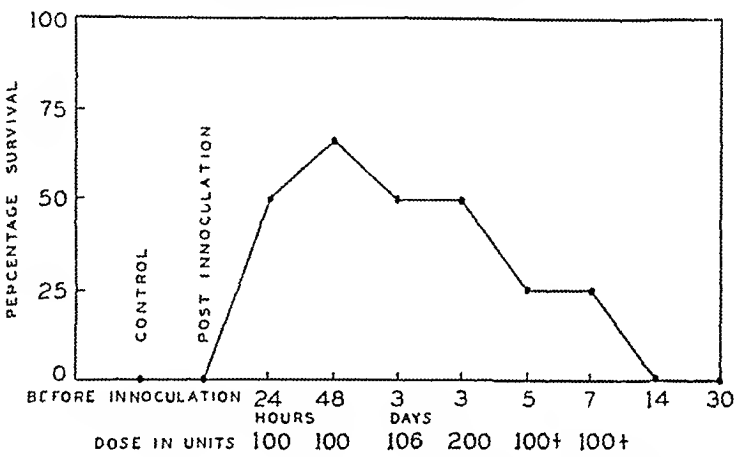
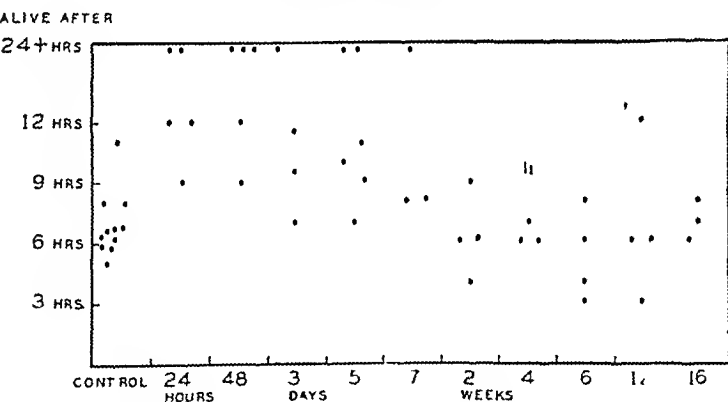


CHART 1—When irradiation was given after inoculation there were no survivors but when given 24 hours prior to inoculation one half of the animals survived. Protection reached a peak in 48 hours and then was rapidly dissipated.

DURATION OF SURVIVAL AFTER INOCULATION AND X RAY THERAPY



PERIOD BETWEEN X RAY AND INOCULATION

CHART 2—From this scattergram it is apparent that the majority of the animals in the groups which received irradiation from 24 hours to five days before inoculation, and died, survived longer than those of the other groups.

Group I—There were six rabbits in this group. Two received a single dose of 100 r, two a total dose of 300 r in three daily doses, and two received a total dose of 600 r, administered in six daily doses. The latter two animals developed diarrhea, from which one died.

Sixteen weeks after the last roentgen ray treatment these animals were inoculated, and four died within eight hours while one survived. Two controls died in six and one-half and eight hours.

Groups II, III, IV and V—These groups differ from the preceding one, only in respect to the intervals of 12, eight, six, and four weeks, respectively, which elapsed between the time of irradiation and inoculation. Eight of the original 24 animals which were irradiated died during the waiting period. The remaining 16 died within 11 hours after inoculation. The three controls died in four, six, and eight hours.

Group VI—There were four rabbits in this group, two received 100 r, and two, 200 r of roentgen ray irradiation in single doses. They were inoculated seven days later, and one of the two, which received 100 r, or 25 per cent of the group, survived. The others died in eight, eight, and nine hours.

Group VII—There were eleven rabbits in this group. Four received 100 r, and four, 200 r of roentgen ray irradiation in single doses, while three were used as controls. Five days later all were inoculated, and two, or 25 per cent of the irradiated animals, survived. The others died in seven, nine, nine, ten, ten, and 11 hours, and the controls died in five, nine, and nine hours.

Group VIII—Eight rabbits were inoculated three days after receiving roentgen ray irradiation (four, 100 r, and four, 200 r). Four (two, two), or 50 per cent, survived. The others died in six and one-half, nine, 11, and 11 hours. Three additional rabbits which served as controls died in five, six, and six hours.

Group IX—Six rabbits were inoculated 48 hours after receiving 100 r of roentgen ray irradiation. Four, or 66.6 per cent, survived and two died in nine and 12 hours. There were three controls, and these died in four, six, and 11 hours.

Group X—Out of six rabbits inoculated 24 hours after receiving 100 r of roentgen ray irradiation there were three, or 50 per cent, survivors. The three fatalities occurred in nine, 12, and 12 hours. The three controls survived only six, seven, and seven hours.

From this series of studies it is apparent that roentgen ray irradiation provided these animals with a considerable degree of protection against the inoculation of the lethal agent. This protective factor conveyed by irradiation was apparent within 24 hours, attained a peak of effectiveness on the second and third days, and then rapidly diminished. The number of animals used in these studies is much too small to provide statistical deductions. The figures have been reduced to percentages merely for purposes of visualizing apparent trends.

Killed Cultures—Because all of the animals became prostrated within two or three hours after inoculation and because those that failed to survive died within 12 hours, and many within the brief period of four hours, an interest in the cause of death was aroused. It seemed unlikely that an infection could establish itself and develop to lethal proportions in such a brief period of time. It seemed probable that there was inherent in the culture, at the time of inoculation, a lethal dose of toxin. To determine the validity of this hypothesis the following studies were carried out with the

same culture, killed by heating in a water bath of boiling water for 12 minutes. The death of the culture was verified by failure of growth on culture media.

Eight rabbits were given intraperitoneal inoculations of two slants of the killed culture in 20 cc of saline. Seven died and one completely recovered. One survived three days, and the others died in seven, eight, eight, nine, 12, and 18 hours.

From this data it seems reasonable to conclude that in the previous experiments with the live culture the animals died not from established peritonitis or from infection *per se* but rather from toxemia, that is an intoxication from the toxic factor which was present in lethal quantity at the time of inoculation.

At this point in the investigation and upon the suggestion of Dr. Alfred Brown, determinations of the hematocrit and quantitative measurements of serum protein were made upon five rabbits before, and five hours after, intraperitoneal inoculation of the killed culture. The first specimens were taken when the animals were in normal health and the second ones when they were prostrated. Because these studies showed the development of the blood changes characteristic of shock, hemoconcentration and hypoproteinemia, with the development of prostration, it seems fair to assume that the state of toxemia produced by both the live and killed cultures was essentially a state of shock. The results of these blood studies are detailed in Table II.

TABLE II

	Serum Protein		M M Packed Red Cells	
	Normal	Inoculated	Normal	Inoculated
1	5.98	4.78	30	34
2	6.47	4.92	31	38
3	5.85	4.62	25	36
4	6.22	5.15	27	36
5	6.15	5.02	30	37
Av	6.13	4.9	28.6	36.2

Obviously, the next problem to be investigated was the effect of prophylactic roentgen ray irradiation upon animals inoculated with the killed culture. Five rabbits were given 100 r each of roentgen ray irradiation, and 48 hours later were inoculated with two slants of the killed culture. Three, or 60 per cent, of the series survived, and two died in 12 and 16 hours. Two additional animals which served as controls died in eight and 12 hours.

With this evidence that prophylactic roentgenotherapy is capable of reducing mortality from the killed culture, there arose the question of the mechanism involved. Is it a local effect resulting from the action of the rays upon the peritoneum or is it a general one?

It had been observed that 48 hours after irradiation the peritoneal cavity contained an increased amount of fluid, and that this fluid was very slightly blood-tinged. Microscopic studies had revealed the presence of

numerous red blood cells but only an occasional white blood cell and plasma cell. It seemed probable, however, that this fluid might contain some element which neutralized the toxin contained in the killed culture. Consequently, four rabbits were given 100 r of roentgen ray irradiation, and 48 hours later were killed. The peritoneal cavity in each instance was opened and washed with 20 cc of saline, which, as it was recovered by aspiration, carried along with it a maximal quantity of the peritoneal fluid. This fluid from each of the four animals was pooled and then mixed with eight slants of the killed culture, and after standing for 30 minutes at room temperature was injected into the peritoneal cavities of four stock rabbits. All, or 100 per cent survived. Two controls, run simultaneously, died within 12 hours.

To determine that this protective property resulted from roentgenotherapy and was not a normal constituent of peritoneal fluid, peritoneal washings from four untreated (stock) animals were obtained, pooled, mixed with eight slants of the killed culture and, after 30 minutes, injected into the peritoneal cavities of four stock rabbits. Three of them died in seven, nine, and 12 hours and one survived. Because this survivor never appeared ill it is possible that the fluid was injected into the lumen of the bowel.

Upon the assumption that the protective factor present in the peritoneal fluid following irradiation might also be present in the blood stream, four rabbits were given 100 r, and 48 hours later were exsanguinated by cardiohemacentesis. The blood thus obtained yielded 84 cc of serum, which was mixed with eight slants of the killed culture and, after remaining for 30 minutes at room temperature, was injected in equal quantities intraperitoneally in four stock rabbits. Three, or 75 per cent, survived, and one died after four days. Two controls died in ten and 14 hours.

The influence of serum from irradiated animals upon the live culture was tested in two rabbits. The procedure differed from that used in the preceding experiment only in that the live culture was used. Both animals survived. A single control died in ten hours.

As in the case of the peritoneal fluid there was the question of the presence of a protective factor in the serum of the normal untreated rabbit. Consequently, the serum from four such animals was mixed with eight slants of the killed culture and, after 30 minutes, was injected into four stock animals. Three died in eight, 14, and 17 hours, and one survived.

The excellent survival record in this last group of experiments may be attributed to the probable fact that the toxicity of the killed culture was much reduced before it was injected, as a result of its contact with the serum or peritoneal fluid for 30 minutes preceding injection. That this serum from irradiated animals contained an antitoxic factor seems a justifiable conclusion and, quite naturally, led to speculation relative to the possibility of using it for passive immunization. The question: Does this serum retain its effectiveness when given subcutaneously or intravenously either previous to, or simultaneously with, inoculation?

Five rabbits were given subcutaneously an equal share (24 cc) of pooled serum obtained from five other rabbits, which 48 hours previously had received 100 r of roentgen ray irradiation. One hour later each animal was given an intraperitoneal injection of two slants of the killed culture suspended in 20 cc of gastric mucin. The interval of one hour between the administration of the serum and the inoculation was allowed to give an opportunity for the absorption of the serum. Three, or 60 per cent, survived, and two died in nine and 16 hours. Five rabbits were given serum intravenously and immediately inoculated. Except for the difference in the route of administration of the serum the technic was the same as that described above. One died while the serum was being given and before inoculation and, therefore, was discarded. Of the remaining four, two, or 50 per cent, survived, and two died. The deaths occurred in 16 and 22 hours. Five animals used as controls for both groups died within ten hours.

It should be noted that the animals which received the serum and failed to survive lived longer than the controls.

To control the interpretation of the results of this series of experiments the same experimental procedure was carried out in six rabbits using normal serum for the subcutaneous injections in place of serum from irradiated animals. Two, or 33.3 per cent, survived, and four died. The fatalities occurred in nine, nine, 11, and 20 hours. There were three rabbits used as controls, and all of them died within nine hours. Although there were only one-half as many survivors in this series as in those in which serum from irradiated animals was used, it is significant that one-third of the animals did survive.

Combined Roentgen Ray and Sulfanilamide Therapy—When it evolved that the killed culture was as lethal as the living one, the failure of sulfonamide therapy became understandable. But after the effectiveness of roentgen ray irradiation became apparent it seemed probable that these two agents might supplement each other and increase the number of survivors. For this reason the following study was made. Ten rabbits were given 100 r of roentgen ray irradiation, and 48 hours later were inoculated with the live culture. Four of them received no further treatment, but each of the remaining six was given 0.5 Gm of one of the two sulfonamides (sulfanilamide and sulfathiazole, three each) in the inoculation fluid. Two, or 50 per cent, of those which received only irradiation survived, while two, or 33.3 per cent, of those which received both irradiation and chemotherapy survived. The fatalities occurred within ten hours. There were two controls. Both died within eight hours. Although this is too small a series for more than a relative comparison, it is obvious that the survival record was not improved by the addition of sulfonamide therapy.

Diphtheria Toxin—All studies, thus far, pertain to one certain culture, alive and killed endotoxin. There arises, therefore, the question of specificity of roentgen ray irradiation for this particular culture and its toxin. As an effort to answer this question a study of the effect of prophylactic irradiation

upon rabbits inoculated with diphtheria toxin* was made. Diphtheria is representative of exotoxins. Its minimal lethal dose for guinea-pigs had been established in the donor's laboratories. This dosage was found to be consistently lethal for rabbits. With this toxin prostration developed more slowly and the animals survived much longer than did those which received the killed culture. The average survival period was 52 hours.

To determine the direct influence of irradiation, 16 rabbits were given 100 r of roentgen ray irradiation, and 48 hours later the diphtheria toxin in 2 cc of water intraperitoneally. Ten, or 62.5 per cent, completely recovered. The average duration of survival of the six that died was 61 hours. Twelve rabbits used as controls and inoculated at the same time, all died. The average survival period was 50 hours.

It is planned to determine the influence of peritoneal fluid and blood serum from irradiated animals upon this toxin, as was done in the experiments with the killed culture. These studies are in progress.

DISCUSSION—Although this study was suggested by a clinical problem it is reported in terms of factual data as observed in rabbits. From this data no direct clinical implications are justified, and none are intended.

As stated previously, it was the purpose of the original problem to determine the effect of the sulfonamide drugs and of roentgenotherapy upon peritoneal infections produced by several different micro-organisms acting both alone and in combination. But this problem was abandoned for the one reported above, after it was learned that the first culture used was as lethal after it had been killed as it was alive, and after the unexpected finding that preliminary roentgen ray irradiation of the animals reduced the mortality from this culture both killed and alive.

Three cultures of hemolytic *E. coli* were obtained from different sources and only one proved to be pathogenic for rabbits. This culture produced within two or three hours profound prostration, which was accompanied in all of the five animals in which blood studies were made by hypoproteinemias and hemoconcentration. Because this state of shock developed so soon, and progressed to a fatal termination so rapidly, following the administration of the killed as well as the live culture, it seems reasonable to assume that death resulted from profound toxemia. Granting this assumption, it follows, then, that the culture contained a lethal quantity of toxin at the time it was injected into the animals. Consequently, any further production of toxin or other lethal factor as a result of growth of the bacteria in the peritoneal cavity was superfluous. If, therefore, the action of the sulfonamides is bacteriostatic, the cause of failure of these drugs to influence the course of events is obvious. This may be the explanation of some failures of these drugs in clinical cases.

When it was discovered that some of the animals which had received roentgen ray irradiation 24 hours to five days before inoculation with the

* This toxin was provided through the courtesy of Eli Lilly and Company.

live culture had recovered, it was thought that recovery might be attributed to the inflammatory reaction of the peritoneum caused by irradiation. This explanation, however, was invalidated subsequently by the observation that preliminary irradiation resulted in an equal number of survivors among the animals given the killed culture. Thus irradiation in some manner lowered mortality from toxemia.

These findings gave rise to the question of mechanism. Did the local inflammation of the tissues incited by irradiation interfere with absorption of the toxins or did the tissues develop some factor capable of neutralizing the toxins? Was the protective factor a local one, present only in the tissues which had been irradiated, or was it a generalized one? It had been observed that the peritoneal fluid was always increased in quantity within a few hours after irradiation. It seemed probable that this fluid might contain a factor capable of neutralizing the toxin and so, 48 hours after irradiation (the optimal period), the peritoneal fluid was aspirated along with the saline used to wash it from the peritoneum. When these washings were mixed *in vitro* with a lethal dose of either the killed or live culture the toxins were sufficiently augmented in each instance to render them incapable of killing the animals. Peritoneal washings from nonirradiated rabbits did not exert this influence.

Since the same augmentation was obtained from an admixture of the live and the killed culture and serum from animals irradiated 48 hours previously, it is apparent that whatever the product resulting from irradiation, it was present in the blood stream and thus generally disseminated. Because one out of four animals survived after receiving a mixture of normal serum and the killed culture, it appears that some rabbits' serum may normally contain the augmenting factor, or that the survival of this animal and, in part, the survival of those which received serum from irradiated animals resulted from the beneficial effect of serum upon shock.

When serum from irradiated animals was given intravenously or subcutaneously prior to intraperitoneal inoculation, the survival record was slightly more than 50 per cent, a better record than that obtained from normal serum used in the same way. It is interesting that the results from the use of serum from irradiated animals are comparable to those obtained in the animals which were inoculated 48 hours after they had been irradiated.

The effect of irradiation given 48 hours prior to the intraperitoneal injection of a lethal dose of diphtheria toxin was determined for the dual purpose of reevaluating with another toxin the observations made thus far, and of determining how specific was the antitoxic factor which resulted from irradiation. A survival record of ten out of 16 rabbits so treated is indicative of the presence of a nonspecific antitoxic substance.

CONCLUSIONS

As an attempt to explain these observations the following theory is offered as a mere suggestion. Roentgen ray irradiation caused injury to

the tissue cells. In response to this insult the cells or some group of cells liberated a protective or antitoxic factor.

Whatever the nature of the protective mechanism, time was required for its development. It was present 24 hours after irradiation—how much earlier is a problem which will be investigated. It apparently developed too slowly, however, to be of benefit to the rabbits which received irradiation after they were inoculated. It reached its peak of effectiveness in 48 hours, and by the seventh day it apparently had been entirely dissipated.

This investigation has given rise to many questions for further study, questions of optimal and minimal dosages of roentgen ray irradiation, the effect of irradiation of portions of the rabbit's body other than the abdomen, and the reaction to irradiation in other animals, *etc*.

THE OPERATIVE REPAIR OF MASSIVE RECTAL PROLAPSE*

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PROLAPSE of the rectum varies in degree from the minor cases in which only the mucous membrane of the anal canal or lower rectum is prolapsed, to the instance of massive prolapse in which the prolapse assumes enormous proportions and includes all the coats of the rectal wall. In the three cases we are reporting, the prolapse started in childhood and had gradually increased in size until it occurred not only during defecation, but also when the patient walked about. In two patients the prolapse assumed such magnitude as to constitute a major disability at age 26. The third case was able to carry on until age 42. It is noteworthy that these patients suffered a progressive increase in the size of the prolapse over many years. In none of the three patients was the prolapse less than six inches in length (Fig 1).

On examining these patients, the most outstanding observation was that the lumen of the rectum presented on the posterior quadrant of the prolapsed mass. The long axis of the lumen was at right angles to the long axis of the body (Fig 2). In Figure 2 the cork in the lumen indicates the site and direction of the canal. This led to the conclusion that the prolapse was more at the expense of the anterior than the posterior rectal wall. The prolapsed mass was resonant on percussion, and, on occasions, gurgling was heard during attempts at reduction. After reduction of the prolapse, the anal sphincter was so stretched that it very poorly closed the anal canal, but in two instances one could see the patient was able voluntarily to contract it. In Case 3 there was no visible evidence of the patient's ability to do so. In two cases there was a definite sulcus about three-quarters of an inch long between the anal canal and the prolapse. In Case 1 no such sulcus was present, the prolapse being so complete that the anal canal was everted. Moschcowitz¹ made an important observation. "If, after reducing the prolapse, the patient strained while the examining finger is pressed anteriorly in the lower rectum, the prolapse would not recur, whereas if pressure were made posteriorly the prolapse recurred immediately."

The disability which these young individuals suffered was very great, not only economically but socially. The problem which they presented to the surgeon demanded careful consideration. Moschcowitz¹ article published in 1912, 30 years ago, advanced the suggestion that a massive rectal prolapse resulted from a sliding hernia of the anterior wall of the rectum at the level of the cul-de-sac of Douglas or rectovesical pouch. Our interest in sliding hernia of the sigmoid² led us to consider seriously this hypothesis. Yet if this be the correct etiology, the treatment suggested by Moschcowitz of

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

plicating the peritoneum of the cul-de-sac of Douglas or rectovesical pouch is inefficient. It would be comparable to plicating the sac of an inguinal hernia without removing it and without any attempt at repairing the defect in the wall.

The injection treatment suggested by Gabriel is comparable to the injection treatment of an inguinal hernia, were one to dispense with the pressure of a truss during the course of treatment. If our observation be sound, that

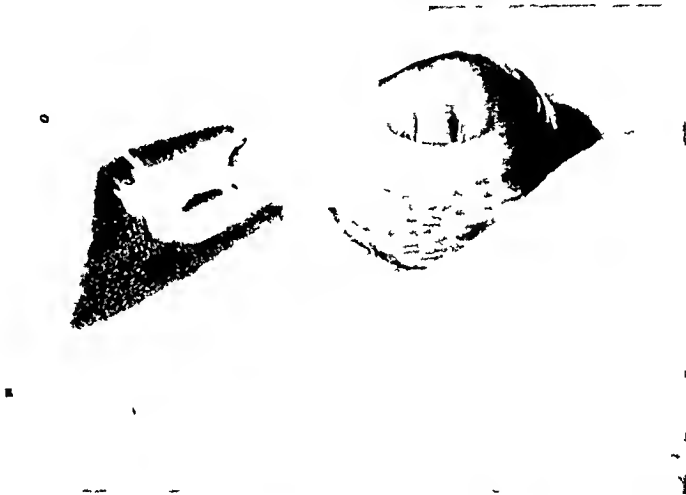


FIG. 1.—The size of the prolapse can be compared to the size of an adult fist.



FIG. 2.—With the patient in the knee chest position the prolapse is seen from behind. The position and direction of the lumen of the rectum is indicated by the cork placed in the lumen.

the prolapse occurs at the expense of the anterior rather than the posterior rectal wall, which is very little disturbed, then the procedure of Lockhart-Mummery and Pemberton is unsound. Their technic is aimed at the fixation of the posterior rectal wall, which is little altered from its normal relationship to the sacrum.

The fact that after reduction of the prolapse, pressure anteriorly by the examining finger in the rectum prevented its recurrence even with straining, was the most important single observation confirming the hypothesis that the lesion was essentially a sliding hernia of the anterior wall of the rectum (Fig. 3).

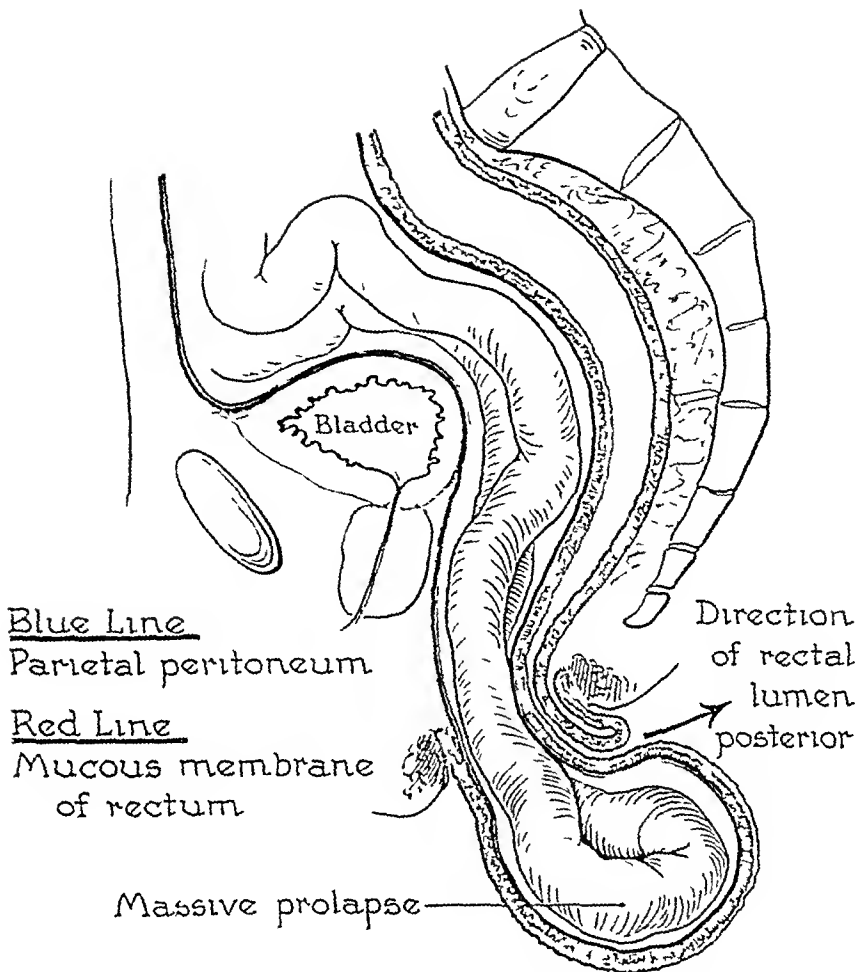


FIG. 3.—The invagination of the anterior rectal wall into itself and through the anal canal separates the fascial and muscular supports of the rectum and by overstretching results in incompetence of the anal sphincter. The lengthening of the mesentery of the small bowel occurs over the years to such a degree that small bowel lies within the hernial sac of a massive prolapse.

In this mechanism the natural defect in the pelvic fascia which permits the passage of the rectum through the pelvic diaphragm is enlarged by the contents of the cul-de-sac of Douglas or rectovesical pouch pressing downward into the anterior rectal wall. This increased bulk of rectum further separates the levator ani by stretching the pelvic fascia, which normally unites them medially. This likewise decreases the normal fixation of the rectum at this level. The separation of the levatoirs permits sufficient anterior wall of the rectum to be invaginated into the lumen of the rectum that the latter pro-

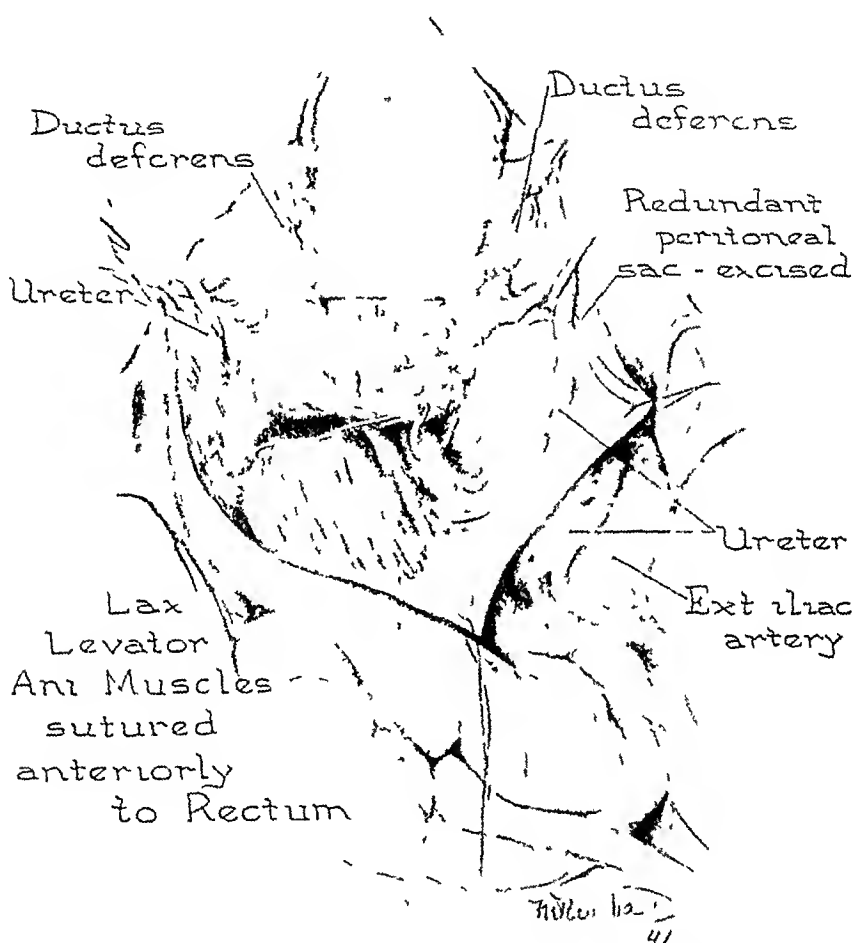


FIG 4—The dissection completed identifies the ureters, the seminal vesicles and the separated levator ani muscles identified by the sutures. They, with the overlying fascia, are approximated with locked mattress sutures of silk. This closure in one case was reinforced by a strip of fascia lata suture.

trudes through the anal canal. As this occurs, the course of the rectum is straightened and the normal angulation of the rectum at the level of the pelvic floor is eliminated. The posterior wall of the rectum is carried forward from the hollow of the sacrum, making the rectum now almost a straight tube, with the fascial supports most inefficient, due to the overstretching. Over the years there has also occurred elongation of the mesentery of the small bowel, permitting the latter to lie in the hernial sac, and this accounts for the tympanic note on percussing the prolapse, as well as explaining the gurgling which was elicited on attempts at reduction.

This conception of the mechanism of production of massive rectal prolapse is not new, nor was it new with Moschcowitz, as it was first propounded

by Jeannell, in 1890 This conception, however, appealed to us so strongly that we felt it pointed a way to safe and adequate treatment, using the same principles as are applied in the operative repair of all herniae, particularly sliding herniae²

If this conclusion be correct, then the adequate treatment should be removal of the sac and repair of the anatomic defect in the wall The anatomic defect is in the pelvic fascia, just as in a direct inguinal hernia the defect is in the transversalis fascia Hence, we must restore the normal relationship of the pelvic fascia to the rectal wall, as well as obliterate the peritoneal sac

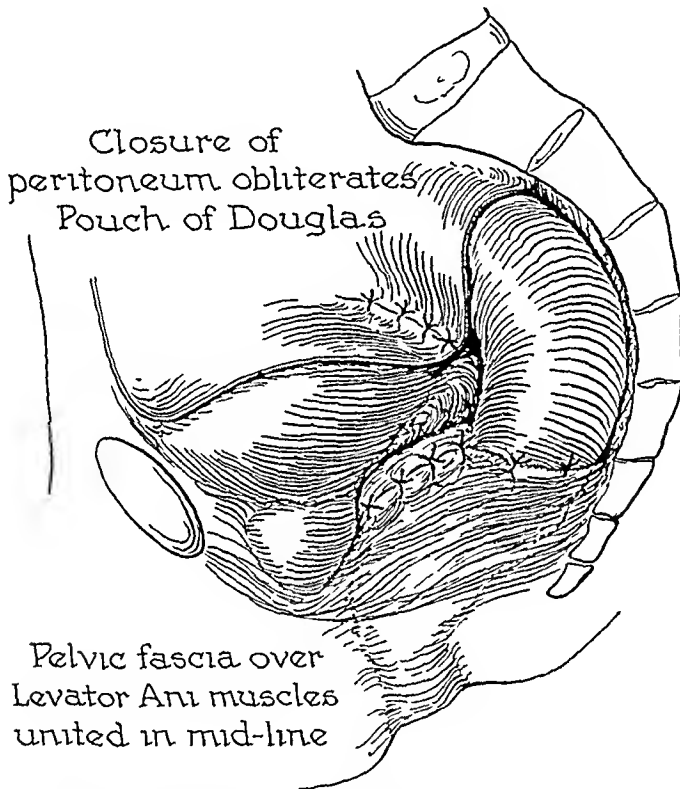


FIG 5.—The levator ani muscles are approximated and their fascial covering united to the rectum by interrupted silk sutures This may be reinforced by sutures of fascia lata This approximation of the levators replaces the rectum in its normal relation to the hollow of the sacrum and prevents the prolapse The redundant peritoneum of the pouch of Douglas is excised and on closing the posterior parietal peritoneum the pouch of Douglas is obliterated

To achieve this, it becomes imperative that we open the peritoneal cavity The following are the details of the operative procedure (Fig 4) With the patient in the Trendelenberg position, under spinal anesthesia, the abdomen is opened by a large incision displacing the lower left rectus laterally The small bowel is packed off with hot sponges Two points were noted First, there was an unusually deep cul-de-sac of Douglas or rectovesical pouch, second, an unduly mobile rectosigmoid, due to the fact that the rectum was pulled forward, had a mesentery throughout the greater part of its length, and did not lie as is usual in close contact with the sacrum Gauze on the

end of a sponge forcep placed on the bottom of the cul-de-sac of Douglas or rectovesical pouch, with downward pressure readily invaginated the anterior rectal wall into the rectal lumen. The defect in the muscular pelvic floor could readily be palpated. This invagination was easily carried through the anal canal, and reproduced the massive rectal prolapse, and convinced us that it really was due to a sliding hernia of the anterior wall of the rectum. Furthermore, this prolapse was readily reduced by upward traction on the rectosigmoid junction. Having convinced ourselves of these facts, the peritoneum of the cul-de-sac of Douglas or rectovesical pouch was opened and dissected free from the extraperitoneal fat and areolar tissue. The ureters were then identified and surrounded with tape, in order to retract them laterally. A further dissection of the perirectal fat made possible the visualization of the seminal vesicles and the widely separated fascial-covered medial borders of the levator ani muscles. With the rectum pulled well up into the abdomen, and starting just behind the prostate, interrupted locked mattress sutures of silk were placed in the fascia covering the levator ani muscles. These sutures united the levators until their resultant approximation forced the rectum back into the hollow of the sacrum (Fig 5). In Case 3 this repair was reinforced by a single suture of fascia lata. This maneuver restored the normal angulation of the rectum. It was then no longer possible to invaginate the anterior wall of the rectum through the anal canal. Pressure exerted at the level of the rectum and new pelvic floor forced the rectum into the hollow of the sacrum, not toward the anal canal. Interrupted silk stitches then united the lateral rectal wall to the fascia over the right and left levators (Fig 5). This appeared to give a very adequate support to the rectum, particularly to its anterior wall, which is so important in preventing a recurrence of the massive prolapse. Excision of the redundant hernial sac and suture of the pelvic peritoneum obliterates the cul-de-sac of Douglas or rectovesical pouch entirely. The abdomen is then closed without drainage.

On return to the ward, the patient remains recumbent, with the foot of the bed elevated ten inches, for one week. A low-residue diet is given. Every effort is made to prevent a stool for a week to ten days, at the end of which time oil enemata are usually effective in producing a stool. The patient is encouraged to practice contraction of the overstretched anal sphincter many times a day, in order that it will regain its tonicity. The following are the details of the three cases.

CASE REPORTS

Case 1—Hospital No A64821 W J P, male, age 26. Admitted April 12, 1939. Mass first present at age six, gradually increased in size, and recently appeared with slight straining when patient was erect. The mass had to be replaced by manipulation. There was marked urgency of defecation.

Examination—The mass was as large as a man's fist, and could be prolapsed voluntarily. In the knee-chest position it could be replaced by violent movements of the abdominal muscles. No ulceration was present. There was no sulcus at the anal sphincter, as the anal canal was also prolapsed. The mass was tympanitic on percussion,

and the lumen of the rectum pointed backward With a finger in the rectum, pressure anteriorly controlled the prolapse

Operation—April 24, 1939 Primary healing, Discharged May 16, 1939 Has had no further trouble, and is doing hard physical work in a tannery at the present time

Case 2—Hospital No A82662 W B, male, age 42 Admitted April 4, 1940 Prolapse first noticed at age eight Now comes down with stool and has to be replaced The size has increased markedly in the previous five weeks Now has a mass 6x8 inches protruding from anus, and reduction becoming difficult (Fig 1)

Examination—Well nourished, sphincter contraction visible and surprisingly good tone The mass is difficult to replace There is no ulceration and no hemorrhage The lumen points posteriorly The mass is resonant on percussion (Fig 2) With a finger in the rectum, pressure anteriorly controlled the prolapse

Operation—April 12, 1940 Had slight superficial wound separation due to coughing from a respiratory infection Good recovery Complete relief, with a very slight prolapse of one area of anal mucous membrane on straining At present is working in munitions plant as a laborer

Case 3—Hospital No A99554 G T, age 26 Admitted April 1, 1941 to the Neurologic Service, with headaches, fainting attacks, and a multiplicity of complaints Only organic finding was rectal prolapse present since childhood Had to be replaced after each stool Marked increase in size of prolapse during past five years, becoming difficult to replace, and on admission prolapse occurs on walking or any exertion

Examination—Sphincter lax No evidence of contraction could be demonstrated by the patient On straining, the rectum prolapsed at least six inches, a sulcus is present between the anal canal and prolapse about one-half inch deep By introducing two fingers into the rectum and pressing anteriorly, the prolapse could be prevented as the patient strained Pressing posteriorly into the hollow of the sacrum while the patient strained, permitted recurrence of the prolapse

Operation—May 10, 1941 Bowels moved on tenth day Primary union Discharged

Progress—No further prolapse of the bowel Slight prolapse of mucous membrane treated by injections of 2 cc phenol and almond oil Some difficulty in controlling stool for four months At present has perfect control of bowel movements On examination, the tone of the sphincter ani is remarkable, but not as strong as normal Her neurologic symptoms have nearly all disappeared She is working in our hospital as a ward aid at the present time We are indebted to Dr Keith Welsh for the privilege of seeing and reporting this third case

CONCLUSIONS

(1) Massive rectal prolapse is a sliding hernia of the anterior rectal wall through the anal canal

(2) The lumen of the rectal canal points posteriorly as the prolapsed mass is formed largely at the expense of the anterior rectal wall

(3) This results in an overstretching of the pelvic fascial supports of the rectum

(4) With the examining finger in the rectum, the prolapse can be controlled as the patient strains if pressure be exerted anteriorly, whereas if pressure be exerted posteriorly, the prolapse will recur

(5) The treatment of this condition should be planned to apply the basic principles underlying the treatment of all herniae—first, remove the sac, second, restore the defect in the wall

(6) A procedure is presented which fulfills these requirements

- (7) It has been successfully carried out on three patients Two have returned to hard labor, the third is working as ward aid in our hospital
- (8) The return of tone in the anal sphincter is most remarkable

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DISCUSSION—DR VERNON C DAVID (Chicago) Doctor Graham has limited his discussion to the type of prolapse of the rectum in which the anus, including the patulous sphincter muscles, prolapses with the four to six inch tube of bowel carrying with it the cul-de-sac of Douglas In principle, the treatment he advocates requires an abdominal approach opening of the cul-de-sac, and the approximation of the levator muscles by suture in front of the rectum He is to be congratulated on the results in the three cases he reports

To present a slightly different viewpoint, I should like to point out that the levator muscles, which have a very delicate fascial covering, completely encircle the rectum and their highest or superior surface is at about the level of the sacrococcygeal junction To tighten these muscles by suture *via* the abdominal approach in the depth of the pelvis is a difficult procedure, and I should like to ask Doctor Graham if he finds it necessary to cut the triangular ligaments of the rectum, which lie below the culdesac, before he reaches the levator muscles When the levator muscles are divided, as in removal of the rectum posteriorly, the rectum is still firmly anchored in place by the fascia propria, which is a dense fascia about one millimeter thick, firmly attached to the sacrococcygeal junction posteriorly and anteriorly to the prostate which it completely envelops Before the rectum can be mobilized this fascia must be cut

It is my belief that it is not only the atrophy and weakness of the levator muscles and depth of the cul-de-sac which favor this type of prolapse but more particularly a weakness and stretching of the fascia which allows the rectum to completely prolapse carrying the cul-de-sac with it In repair of this type of prolapse we, therefore, believe that the structures in most need of support are in the prolapsed segment of bowel and on its outer surface, namely, the fascia propria and levator muscles We also believe that the atonic sphincter muscles, which have been greatly dilated by the prolapse of the bowel and levator muscles through them, are a factor which favors early recurrence of the prolapse

With these anatomic facts in mind I should like to call your attention to the operation for the repair of this type of prolapse originally proposed by Delorme, in 1890, and first carried out by Rehn, in 1896 This operation is easily carried out under novocain anesthesia and consists in the removal of the mucosa of the prolapsed segment from the mucocutaneous line to the apex of the prolapse The muscularis of the bowel, levator muscles, and fascia propria in the outer layer of the prolapse are collapsed like a closed accordion by longitudinal puckering-stitches, which reduces the prolapse and makes tighter the supporting levator muscles and fascia propria and places the puckered mass of muscle and fascia above the sphincter muscles, which are narrowed below it by angulating stitches The excess of freed mucosa is then cut off and the cut surface sutured to the skin This operation accomplishes everything but obliteration of the cul-de-sac I first saw Doctor Bevan perform this operation, and I have carried it out in 12 cases, with good results, and no massive recurrences In women, where the perineal body is gone and the levator muscles are widely separated it is advisable to perform a later perineorrhaphy

This type of prolapse demands, essentially, strengthening of the pelvic fascia and levator muscles In my opinion this may be best accomplished by the abdominal operation described by Bardenheuer, Moschcowitz, and Graham, or by the Rehn-Delorme operation from below

DR CHARLES G MIXTER (Boston) Massive rectal prolapse, particularly of the recurrent variety, is frequently a discouraging lesion from the surgeon's viewpoint Doctor Graham has presented to us a well-conceived operation that has been successful in the

three patients he has subjected to this procedure, and in skilled hands it should yield good results. It is, however, a procedure of considerable magnitude. The lesion occurs many times in the aged and, perhaps, enfeebled group. It might not be amiss to bring before this Association briefly a simple procedure that has yielded satisfactory results in the two cases upon whom I have had the opportunity to try it.

The abdomen is opened through a low left rectus muscle-splitting incision. A small opening is made in the pelvic floor on either side of the rectosigmoid. The rectum is mobilized by blunt dissection and cigarette wicks are inserted to stimulate fixation of this bowel segment by resultant fibrosis. The wicks are brought out through stab wounds above the inguinal ligament on either side. Further experience may prove this step to be unnecessary. The sigmoid which is usually redundant is brought out of the abdominal wound in a manner similar to a subcutaneous loop-colostomy or precolostomy. The distal limb of sigmoid should run tautly downward from the lower angle of the wound to the rectosigmoid. The proximal sigmoid reenters the abdomen at the upper end of the incision. All layers of the abdominal wall except the skin and superficial fascia are closed in a routine manner beneath the exteriorized sigmoid through an opening established in the mesentery. The fat is separated from the anterior rectus sheath and allowed to gape to accommodate the loop and the skin is closed over the bowel. Care must be taken not to constrict the lumen where the bowel enters and leaves the abdomen.

Two cases both having had three previous procedures, have been treated by operation based on the principle of fixation of the sigmoid in the abdominal wound. In the first case, a woman of about 40 a double-barrel colostomy was done, the bowel later opened, the spur crushed and the colostomy closed. This patient has remained free of recurrence and with satisfactory bowel function for two and one-half years. The second case was a rather feeble woman in the late sixties, who was operated upon by the method outlined above. She had no difficulty in moving her bowel postoperatively. It is now about nine months since operation and I understand she has had no recurrence though I have not had an opportunity to examine her personally.

The results in two cases are insufficient to draw conclusions from, but suggest that this simple procedure may be worthy of further trial, particularly where relief must be given in the poor-risk group.

DR JOHN PEMBERTON (Rochester Minn.) Since Doctor Graham mentioned the operation that I described four years ago I would like to run over, very briefly the principles of it, which are similar to what Doctor Mixer has described.

I think the fundamental principles of rectal prolapse are about the same that you see in the colostomy. If the distal segment or the segment just distal or just proximal to the colostomy is fixed you will not get a prolapse of the colostomy if you get up close to the descending colon but if you take it in the middle of the sigmoid, then you are very likely to get a prolapse.

You cannot make a complete fixation of the rectum unless you divide the pelvic peritoneum so this is done either on one side or both sides. Then the rectum is freed up from the segment going down there. This permits fibrosis to take place here which you can readily determine by examining the rectum digitally after incision. This is freed up and we get a space between the rectal wall and the sigmoid, until it heals. The problem is of course to suspend the sigmoid afterward. The suspension will not hold but if it holds temporarily, for a couple of weeks I believe the fixation will hold up.

Four years ago I reported six cases that we had operated upon. I think the longest case was two or three years. Since then we have done others, but of those six cases I know that one has had some recurrence of the prolapse.

DR ROSCOE R GRAHAM (closing) I have just one thought and that is to state our amazement at what happened at the anal sphincter. In the patient whom you saw in the moving picture there was no visible evidence, whatsoever, that the patient could make the slightest contraction of the anal sphincter. That was a year ago. At the present time by encouraging her to voluntarily attempt contraction, she has an anal sphincter which is not as good as normal but is amazingly good in its grip of the examining finger. The other two men had visible evidence at the time of operation and they have come back with exercise in a way that is remarkable. While one is conscious of the fact that this is a major procedure it also is undertaken to correct a very major disability.

TESTS OF HEPATIC AND PANCREATIC FUNCTION IN THE DIFFERENTIAL DIAGNOSIS AND PREPARATION OF PATIENTS WITH LESIONS OF THE BILIARY TRACT*

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THE VITAL RÔLE of the liver in the formation of prothrombin is indicated both by animal experiments and by clinical studies. Thus, Smith, Warner and Brinkhous¹ observed a precipitous fall to less than 10 per cent of normal within 24 hours after chloroform anesthesia, and a return to normal after six days. Warner² removed about two-thirds of the liver of the rat and noted a lowering of the plasma prothrombin, followed by recovery as the hepatic tissue regenerated. Wairen and Rhoads,³ and Andrus, Lord and Moore⁴ independently performed total hepatectomy in dogs and found that the plasma prothrombin fell progressively to levels almost too low to measure after 12 to 16 hours. The latter authors also demonstrated that even massive doses of vitamin K were ineffective in elevating the plasma prothrombin of the hepatectomized dog. More recently, Brinkhous and Wainer⁵ have confirmed the ineffectiveness of the vitamin after chloroform intoxication.

Bollman, Butt and Snell,⁶ studying chronic hepatic injury produced in rats by means of carbon tetrachloride vapor, were able to demonstrate depression of the plasma prothrombin levels as well as the failure of vitamin K to bring about improvement. These authors also noted that a diet rich in carbohydrate delayed the onset of hepatic damage and prolonged the lives of the animals by as much as 50 per cent.

Many observers⁷⁻¹⁴ have stressed the fact that the level of the plasma prothrombin is depressed in patients with hepatic disease and that under such circumstances the response to vitamin K therapy is inadequate or even absent. As yet, there is no correlation between the type of hepatic damage and the response to the vitamin, but most workers are in agreement as to the fundamental connection and as to the increase in the response as the condition of the liver improves.

These facts have suggested the use of the level of the plasma prothrombin and its response to vitamin K as an index of liver function. Thus, Pohle and Stewart,¹³ in 1940, were the first to publish experience with such a method, suggesting specifically the response of a depressed level of plasma prothrombin as measured by Quick's test to the administration of vitamin K and bile salts by mouth as a satisfactory method. In their series of 46 jaundiced patients with reduced plasma prothrombin, 28 showed satisfactory response while in 18 the level failed to improve. Wilson¹⁵ put forth the idea

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that the level of the plasma prothrombin might be considered as an index of hepatic function, and in 36 cases found a close correlation of this value with the results of the hippuric acid test

However, both the above methods are subject to certain errors. Pohle's and Stewart's method may give inaccurate impressions because of possible failure of absorption from the intestine in the presence of disease of the digestive tract and in the rare but definite instances of defective absorptive mechanisms. Wilson's employment of the level of the plasma prothrombin fails to take into account the other factors aside from liver damage which may cause lowering of the prothrombin level.

Since October, 1939, we have studied the application of the level of plasma prothrombin and its response to intramuscular 2-methyl-1, 4-naphthoquinone as a measure of liver function in some 86 cases, and with certain restrictions find it perhaps the most accurate method available. We prefer the parenteral route—intramuscular in all our own cases—for the reason that we have encountered at least two otherwise normal individuals in whom, despite the presence of bile in the intestine and apparently normal liver function by several tests, the plasma prothrombin was depressed to about 60 per cent of normal and could not be elevated by vitamin K administered by mouth with or without bile salts. Intramuscular injection was followed by a prompt elevation to normal. This we can only explain by postulating a defective absorption from the intestinal tract.

We, therefore, have adopted the thesis—which is well borne out by clinical data to be presented below—that the level of the plasma prothrombin if below 80 per cent in a given case is an index of the performance of the liver while the response to 2 mg of 2-methyl-1, 4-naphthoquinone administered intramuscularly indicates whether any depression of this function is or is not due to organic liver disease.

We have compared this method with the galactose tolerance, hippuric acid and bromsulfalein clearance tests in three groups of selected cases. In a group of seven patients with Laennec's type of cirrhosis of the liver the plasma prothrombin failed to rise by more than 6 per cent after the intramuscular injection of 2 mg of menadione. This failure to respond, we feel, indicates intrahepatic disease of a significant degree, but prognosis is only possible when the test is employed on several occasions and the trend observed. The galactose tolerance test was used in six of the seven patients with cirrhosis of the liver, and was abnormal in only four. The hippuric acid test was less accurate than the galactose tolerance test, being below 100 per cent (3 Gm) in only two out of five of the cases. The bromsulfalein test stood last in point of accuracy with three normal results in three cases of cirrhosis.

In a group of nine cases with catarrhal jaundice the plasma prothrombin test showed impaired hepatic function in seven instances, and in general paralleled the severity of the disease. The galactose tolerance test was equally accurate in this group, showing greater than 3 Gm excreted in seven out of nine patients. The hippuric acid test was abnormal in three out of seven

cases, while the bromsulfalein test was abnormal (10 per cent retained) in one case of catarrhal jaundice proved at operation, in which the other three tests were normal

The third group of patients studied suffered from obstructive (extrahepatic) jaundice due to a variety of lesions. The plasma prothrombin response was good in all of 11 cases in which it was used, while the galactose tolerance test was normal in only six out of nine cases. The hippuric acid test was normal in seven out of eight, and the bromsulfalein test was normal in all four cases in which it was used. In this group of patients with extrahepatic jaundice the question arises as to whether the impairment of hepatic function as determined by the galactose tolerance test is or is not significant. If significant, then the plasma prothrombin test is less sensitive in this group than the galactose tolerance test. It seems clear that the bromsulfalein test was the least sensitive in each of the three groups of cases and that the plasma prothrombin and galactose tolerance tests yield the most significant results. The hippuric acid test falls between the galactose tolerance test and the bromsulfalein test in point of accuracy.

An important application of liver function tests is in the field of differentiation between obstructive jaundice of intrahepatic and extrahepatic origin. Such differentiation is frequently possible because the intrahepatic lesions causing jaundice, such as catarrhal jaundice, cirrhosis, *etc.*, are associated with liver damage, whereas in obstructive jaundice due to choledocholithiasis, injection and edema of the common duct or tumors of the pancreas the liver is usually normal unless the jaundice is of long standing. A wide variety of tests have been used to this end but only a few have stood up under rigid clinical application.

The galactose tolerance test was employed by Shay and Schloss,¹⁶ and by Schiff and Senoi,¹⁷ who reported excellent results, but Banks, Sprague and Snell¹⁸ found the test of no real value in the differentiation of the two types of cases. Recently Bassett, Althausen and Coltrin,¹⁹ using a modification of this test, found that 82 per cent of a group of patients with extrahepatic obstruction of the common duct had less than 20 mg per cent of galactose in the blood 75 minutes after injection, while 81 per cent of those with parenchymatous jaundice showed blood levels above this figure. In 18, or 19 per cent of the cases, therefore, the test failed to give an accurate diagnosis.

The cephalin-cholesterol flocculation test of Hanger²⁰ has been highly accurate in the hands of its inventor, being correct in 58, or 92 per cent, of 63 cases. Rosenberg²¹ confirmed this finding, and observed that in jaundice of recent origin a strongly positive flocculation test indicated an intrahepatic origin, while a negative or faintly positive test suggested an extrahepatic cause for the jaundice. Pohle and Stewart,²² however, found the test unsatisfactory in the differential diagnosis of jaundice, as it was strongly positive in six of 23 patients with obstructive jaundice of extrahepatic origin.

Loid and Andrus²³ have used the response of the plasma prothrombin

level to menadione administered intramuscularly as a means of determining the site of origin of obstructive jaundice and obtained a high degree of accuracy. Thus, it was correct in 32 of 36 cases of intrahepatic jaundice and in 49 of 50 cases of extrahepatic obstruction of the common duct, an over-all accuracy of 94 per cent. There were 20 additional cases of extrahepatic jaundice, not included in the above group, whose initial prothrombin level was over 80 per cent, a finding which, when present in jaundice, has always indicated it to be of extrahepatic origin.

The technic employed was as follows. Determinations of the level of plasma prothrombin are made on two successive days by the Warner, Brinkhous and Smith test,²⁴ and if the two levels are within 5 per cent of each other, 2 mg. of menadione are injected intramuscularly, and the prothrombin is determined at intervals of 24, 48 and 72 hours. On the other hand, if there is a difference greater than 5 per cent in the two initial levels of prothrombin, the level is determined on the third day, and so on, until the levels on two successive days are found to be within 5 per cent of each other. When such agreement occurs, then the menadione is administered. On no occasion have we found it necessary to determine the prothrombin for more than three successive days before injecting menadione.

Lake, using a modification of the method of Agren and Lagerlof²⁵ for measuring the external secretory function of the pancreas, with intravenous secretin as the stimulus, has studied about 34 patients including a number of cases of obstructive jaundice. Agren's and Lagerlof's method has also been employed by Diamond and Siegel,²⁶ and by Pratt, Brugsch and Rostler.²⁷ The method consists, essentially, in obtaining duodenal secretion by means of a double lumen duodenal tube and, after collecting a control sample, injecting secretin intravenously. Further samples are collected ten, 20, 40 and 60 minutes later, and the total volume of secretion together with the sodium bicarbonate, trypsin, diastase and lipase content measured. The average and minimal normal values are as follows:

	Average	Minimal
Volume cc	203 cc	94
Bicarbonate		
Highest concentration	99.6	76 milli equivalents
Total output	151	62 $\left(\frac{N}{10} \text{ NaHCO}_3 \right)$
Diastase	432	238 units per 60'
Trypsin	47	20 units per 60'
Lipase	12,260	6,000 units per 60'

By means of the combined use of the response of the plasma prothrombin level to intramuscular menadione and a study of the amount of pancreatic ferments in the duodenal contents, it has been possible to localize some of the lesions causing obstructive jaundice with a high degree of accuracy. The first of the following cases demonstrates the application of these tests in the diagnosis of carcinoma of the common duct not involving the ampulla, while the second indicates a possible source of error in the presence of an aberrant pancreatic duct.

Case 1—N Y H No 309635 J M, male, age 70, entered the hospital complaining of jaundice and itching of the skin of six weeks' duration. The family history and past history were noncontributory. The salient features of the present illness began six weeks prior to admission and consisted of jaundice, itching of the skin and clay-colored stools. The jaundice persisted without remission, and over the past six months there had been generalized weakness and a loss of 35 pounds in weight, with poor appetite. Bowel movements had been regular and there had been no bloody or tarry stools.

Physical Examination—The patient was a well preserved, deeply jaundiced male who appeared acutely and chronically ill. The skin, aside from the jaundice, showed many scratch marks over the trunk. A grayish, raised area was seen on the anterior thorax in the third interspace, and over the spinous process of the third lumbar vertebra was a large sebaceous cyst 3x2x3 cm. There was no lymphadenopathy and the heart and lungs showed no abnormalities.

Abdominal examination showed the wall to be soft and relaxed. The liver was palpable 7 cm below the costal margin in the midclavicular line, and was smooth and soft in consistency. Two large inguinal herniae extending into the scrotum were evident. The remainder of the physical examination, except for a moderately enlarged prostate, was negative.

Laboratory Data—On admission. Urine—sp gr fixed between 1.012 and 1.016, albumin 2+, 8-10 W B C per high power field, occasional hyaline cast. Bile pigments were present in the urine. Blood—hemoglobin, 11 Gm, R B C 3 million, W B C 8,200, with normal differential. Kline negative. The B U N varied from 17 to 64. Blood sugar 63, chlorides 400 on one occasion and 540 on another. The serum protein varied from 5.7 to 7.0. Icteric index on admission, 112, rising later to 187. The stools were negative for bile. G I series was negative. Chest film showed an elongated and tortuous aorta and slight pulmonary emphysema. The plasma prothrombin level was 38 per cent of normal on admission, falling to 18 per cent on the second day. The administration of vitamin K was promptly followed by a rise to 73 per cent, which subsequently reached 100 per cent on one occasion, and remained above 66 per cent at all times.

Studies of the pancreatic secretion showed the following:

Volume cc	187 cc
Highest bicarbonate level	114 milli equivalents
Total output	152.5 $\left(\frac{N}{10} \text{ NaHCO}_3\right)$
Diastase	149 7 units per 60'
Trypsin	34 units per 60'
Lipase	12,747 units per 60'

This indicated a normal response, except for a somewhat low diastase value resembling the results seen in pancreatitis.

The normal response of the plasma prothrombin level to intramuscular menadione was strong evidence that the jaundice was due to obstruction of the common duct, and the presence of normal amounts of the external secretion of the pancreas indicated patency of the pancreatic duct. The obvious diagnosis was, therefore, an obstruction of the common bile duct above the ampulla, and, at operation, a hard, nodular tumor mass was found extending from the junction of the cystic and common ducts down to the duodenum but not involving the ampulla. Cholecystojejunostomy was performed, which functioned only temporarily as bile was present in the stools for only a few days. He died on the twenty-third postoperative day, and at postmortem examination the growth was found to have extended to involve the cystic duct, thereby preventing the cholecysto-enterostomy from functioning.

Case 2—N Y H No 311583 J B, male, age 57, had complained of jaundice and itching for four weeks. The family and past histories were irrelevant to the present illness. This began about six months previous to his admission, when he experienced four or five episodes of epigastric fullness coming on shortly after eating, and lasting for about

two hours. Following this he had no further symptoms until about four weeks before entering the hospital when he had diarrhea for one week, passing ten to 12 stools a day, which were light in color. At this time his appetite became poor and he began to note the yellowish discoloration of his skin. The jaundice deepened steadily and was associated with itching, dark urine and clay-colored stools. He became more easily fatigued, and lost 20 pounds in weight.

Physical Examination—The patient was well-developed and well-nourished, deeply-jaundiced, and in obvious distress because of itching of the skin. The positive findings centered in the abdomen, where a mass was felt in the upper quadrants which extended about five fingers' breadth below the right costal margin. This was quite obviously an enlarged liver and, extending from beneath it for about 8 cm, there presented a rounded, smooth, nontender mass representing an enlarged gallbladder.

Laboratory Data—On admission Urine—sp gr 1.012 to 1.020. Blood—hemoglobin 10 Gm, RBC 3.8 million, WBC 9,000, differential not remarkable. Blood chemistry: Sugar, 78, urea nitrogen, 11, icteric index, 100, serum proteins, 6.6, chlorides, 620, CO₂ combining power, 52.

The study of the pancreatic secretion from the duodenal drainage showed

Volume cc	501 cc
Highest bicarbonate level	96 milli equivalents
Total output	382 $\left(\frac{N}{10} \text{ NaHCO}_3\right)$
Diastase	673 units per 60'
Trypsin	115 units per 60'
Lipase	11,886 units per 60'

These results indicated an extremely active pancreatic response to secretin, much higher in all respects than the average normal values.

At operation, a tumor was found involving the second portion of the duodenum, the region of the ampulla and the inferior portion of the head of the pancreas. The head and body of the pancreas, together with the entire duodenum to a point beyond the ligament of Treitz, was resected. The remainder of the pancreas was implanted into the open end of the jejunum and an antecolic gastro-enterostomy and cholecysto-enterostomy performed. The patient has recovered and is apparently well three and a half months later.

Examination of the specimen revealed a carcinoma of the duodenum invading the pancreas and obstructing the ampulla. There was a very large accessory pancreatic duct emerging about 5 cm proximal to the ampulla, explaining the presence of pancreatic enzymes in the duodenum.

The presence of such aberrant ducts may vitiate the accuracy of the secretin test in localizing obstructive lesions and the case (Case 2) herewith reported demonstrates the possibility of misleading results from this cause.

During the past decade, the condition of the liver has been studied in a variety of surgical diseases, such as gallbladder disease, obstructive jaundice, and hyperthyroidism, with the result that renewed interest has been directed toward factors which maintain and improve hepatic function. Coincident with these studies, there has been much clinical and experimental work on cirrhosis of the liver. Although much remains to be learned concerning the pathogenesis of cirrhosis, its prevention and treatment, and the optimal means of protecting the liver or of improving the function of the already damaged organ, significant information has been forthcoming.

Thus, the effect of anoxemia in producing hepatic damage has been demon-

strated by Rich,²⁸ and by Goldschmidt, Ravdin and Lucké,²⁹ and its clinical significance has been emphasized by Judd, Snell and Hoerner.³⁰ Selection of the proper anesthetic in patients with diminished liver function, and the liberal use of oxygen therapy during the postoperative phase, is of great importance in preventing further damage to the liver, both in conditions such as hyperthyroidism, in which oxygen requirements are increased above the normal, and in patients with pulmonary complications or anemia, which may exert anoxic effects on the hepatic cells.

The deleterious effects of mechanical trauma to the liver as reflected in the plasma prothrombin level has been demonstrated experimentally in the dog,^{31, 32} emphasizing the necessity for handling the liver as little as possible during operations.

However, most important for the prevention of hepatic damage and for the improvement in function of an already impaired liver is careful dietary management of the patient. For more than 30 years, experimental and clinical studies on the relation of various food factors to the liver have been carried out, and recently significant facts have emerged. The favorable influence of a high carbohydrate diet on the liver of rats to which chloroform had been administered and the adverse effect of fat in the diet was demonstrated by Opie and Alford.³³ Several workers confirmed the above findings, but recently Goldschmidt, and his coworkers,³⁴ observed that the proportion of fat in the liver was of more significance in its susceptibility to injury than the amount of glycogen present. They postulated that fat in the hepatic cell acts as a site of retention for the chloroform and, by fixing this circulating toxin, causes degeneration and necrosis. By increasing both the fat and glycogen content of the liver simultaneously they were able to show that such an organ was exactly as susceptible to injury as one in which only the fat content was elevated. In other words, the beneficial effects of glycogen were indirect, through displacing the fat in the liver cells and sparing protein.

The rôle of protein and its influence on the liver has been a subject of considerable controversy, but certain definite conclusions are now possible as a result of recent work by Ravdin, and his associates, and by Whipple, and his coworkers. Bollman and Mann³⁵ claimed that protein in the form of meat was almost as harmful to the survival of dogs intoxicated with repeated small doses of carbon tetrachloride as was a high fat diet, and believed that it was not the protein *per se*, but rather the water soluble extractives in meat which were the responsible agents. On the other hand, Messinger and Hawkins³⁶ found that a high protein diet (meat in the form of hamburger) was most effective in preventing hepatic injury when intravenous arsphenamine was employed as the hepatotoxin. Davis and Whipple³⁷ reported that skimmed milk and casein have a marked protective action on the liver against chloroform, while skeletal and cardiac muscle were far less effective. Goldschmidt, and his coworkers,³⁴ also submit evidence of the importance of protein in the protection of the liver against chloroform, pointing out that protein has the following four modes of action: (1) Probably some specific, and as yet un-

known action on the liver cell, (2) by displacing fat more effectively than carbohydrate, thereby making the liver less susceptible to injury, (3) through the fact that the liver is one of the chief storehouses of protein, and (4) by playing the major rôle in the regenerative phase, which begins within 72 hours of the original injury to the organ. The above authors established the fact that protein causes a decrease in the fat content of the liver better than does carbohydrate both in rats poisoned with chloroform and in dogs with obstructive jaundice^{34, 38}. Lord, Andrus and Moore³⁹ confirmed the efficacy of a high carbohydrate, high protein (milk as the source of protein), low fat diet in dogs with obstructive jaundice, demonstrating that animals on this carefully controlled diet lived an average of 75 days, in contrast to a group of dogs which lived an average of 47 days when kept on a regular balanced laboratory diet.

Miller, Ross and Whipple⁴⁰ have recently shown that methionine and cystine have a marked effect in protecting the liver against chloroform anesthesia in dogs with hypoproteinemia. They believe that the specific action of these amino-acids is due to their SH* groups which tend to spare the normal enzymes associated with the oxidation-reduction system in the hepatic cells (glutathione, etc.). It is their opinion that chloroform produces its toxic effect by injuring these enzymes, and that an excess of SH* groups as in cystine and methionine spares the cells in the presence of the toxic agent. Since the milk protein, casein, is high in these amino-acids, it seems likely that the specific effect of protein, postulated by Goldschmidt, and his co-workers, may rest on the same basis.

In addition to the above factors, the significance of total caloric content of the diet has been emphasized by Ravdin, and his co-workers,⁴¹ who found that a high caloric, general diet was of greater value in lowering the lipid content of the liver than was the intravenous administration of glucose alone. In fact, animals on the intravenous glucose regimen actually showed a small increase in the lipid content of the liver. From this study the importance of a diet adequate in caloric intake becomes evident.

Finally, perhaps the most significant findings, in the experimental work on the influence of diet on hepatic function and structure, concern the importance of certain vitamins and vitamin-like substances to the liver. Best, and his associates,^{42, 43, 44} have reported an extensive study on the effect of choline on the metabolism of fat in the liver and have shown that this substance in amounts as small as 5 mg per day will cause a decrease in lipid content of the liver of a rat on a high fat diet, and will also prevent the deposition of fat under similar circumstances. On the other hand, these workers were unable to demonstrate that choline had any protective action against fatty degeneration of the liver of rats poisoned with either phosphorus or carbon tetrachloride, although it was most effective in clearing fat from the liver poisoned with these agents. Miller, Ross and Whipple⁴⁰ confirmed the work of Best,

* SH=sulphydryl

and his coworkers,^{43, 44} finding that lecithin (5 Gm per day) for three days before chloroform anesthesia, in protein depleted dogs, failed to protect the liver. Goldschmidt, Vars and Ravdin,³⁴ also, are quoted by Miller, Ross and Whipple,⁴⁰ to the effect that choline was of no value in the protection of the liver.

Forbes, Neale, and their associates,⁴⁵⁻⁴⁹ have isolated a crystalline substance from hog liver having a markedly protective action against chloroform and carbon tetrachloride in rats. They subsequently identified the substance as xanthine, and demonstrated that its action is neither on the fat content of the liver nor on the lipid level of the blood. Forbes, Leach and Outhouse⁴⁹ believe that the susceptibility to carbon tetrachloride poisoning is not related to the lipid content of the liver but rather to the active metabolism of fat in this organ.

Experimental necrosis and cirrhosis of the liver also have been produced in the rat⁵⁰ and rabbit,⁵¹ using special diets which were deficient chiefly in the B complex, Rich and Hamilton⁵¹ finding that rabbits fed a diet adequate in every respect except for the B complex developed cirrhosis of the liver in from 25 to 113 days. If all of the then known synthetic vitamins of the B complex were added, including thiamine, nicotinic acid, riboflavin and B₆ (pyridoxine), the cirrhosis still occurred. If, however, whole brewers' yeast was administered, the changes in the liver were prevented. Kensler, and his associates,⁵² using butter-yellow (dimethylaminoazobenzene) in the diet of rats have produced carcinoma of the liver in 96 per cent of the animals in an average of 150 days, but this was regularly prevented by the addition of whole brewers' yeast. However, prevention by nicotinic acid and riboflavin was accomplished only in the presence of large quantities of those two synthetic vitamins, while riboflavin and casein showed excellent protection (seven per cent of the rats). Recently, DuVigneaud, and his coworkers,⁵³ have found that the addition of biotin increases the incidence of carcinomata of the liver in rats fed butter-yellow and "breaks through" the protective effect of diets containing riboflavin, casein and choline. It is significant that cirrhosis precedes the development of the neoplastic process in these animals.⁵²

Further evidence of a protective factor in the B complex was adduced by Drill and Hays,⁵⁴ who showed that normal liver function as measured by the bromsulfalein test can be maintained in dogs when thyroid extract was administered, while impairment of hepatic function occurred regularly despite an adequate diet, unless supplemented with brewers' yeast.

Daft, Sebiell and Lillie⁵⁵ were able to produce cirrhosis of the liver in rats on a special diet and could prevent it by adding casein (30 per cent of the diet), methionine (0.7 per cent of the diet) or choline (20 mg daily) either singly or in combination.

We⁵⁶ have studied the protective effect of a number of substances against minimal liver damage by what appears to be a very sensitive method. A description of the technic follows. Normal adult dogs weighing about 10 Kg,

which have been kept on the regular balanced laboratory diet, are injected subcutaneously with minute amounts (0.03 to 0.24 cc per Kg) of chloroform dissolved in mineral oil, and plasma prothrombin determinations by the method of Warner, Brinkhous and Smith²⁴ are carried out before injection, and every 24 hours thereafter, if possible, for one week. The 24- and 48-hour samples are the most important. Although there may be a wide range in the fall in the plasma prothrombin following the injection of any given amount of chloroform—animals new to the laboratory usually show a greater fall in the level of plasma prothrombin after the injection than animals which have been in the environment of the laboratory for several months—in general, a relatively constant fall occurs from animal to animal when the same amount of chloroform is used.

Plasma Prothrombin in Per Cent of Normal

Chloroform Cc per Kg	Preinjection	Postinjection	
		24 Hour	48-Hour
0.03	100	75	80
0.12	100	50	60
0.24	100	30	< 3

Only an occasional acclimated dog shows jaundice when 0.24 cc per Kg of chloroform is injected, and most animals survive 0.5 cc and 1.0 cc per Kg amounts. This finding is in contrast to the effects of 20 minutes of light chloroform anesthesia, as described by Miller, Ross and Whipple⁴⁰ as their standard dose, which caused jaundice and often death in the control animals. Our dosage—0.12 cc to 0.24 cc per Kg—is four to six times smaller. In normal dogs,¹ 90 minutes of deep chloroform anesthesia does not usually kill the animal, although jaundice appears and the prothrombin and fibrinogen levels fall to very low levels. Barrett, and his coworkers,⁴⁴ in their experiment on the effect of choline on the liver, when carbon tetrachloride was used as the hepatotoxin, employed 0.7 to 0.8 cc of carbon tetrachloride per rat (200 Gm) which is approximately 30 to 40 times the amount per unit weight which we use in the dog. When we use such minimal doses we find that protein added to a well balanced diet in a normal dog is less effective in conferring added protection to the liver. Thus, casein was fed to dogs in 13 Gm per Kg amounts per day, for three days (the standard feeding period), with only slight beneficial effect, the treated animals showing almost as great a fall as the controls.

Attention was then directed to certain factors in the B complex. It was found that thiamine (2 mg per Kg), riboflavin (0.5 mg per Kg), and nicotinic acid (14 mg per Kg) were without protective effect in the doses used. On the other hand, whole brewers' yeast (1 Gm per Kg) was effective to a significant degree, the fall in the plasma prothrombin being cut approximately in half. Also, the return of the prothrombin to normal was hastened from seven days—the usual time for recovery—to five days on the average. Our experiments indicate that the protective action of a single dose of 1 Gm per Kg of brewers' yeast begins to be lost by the end of 24 hours.

Choline was found to have a greater protective action than any other individual substance and was quite as effective as whole brewers' yeast

		Plasma Prothrombin in Per Cent of Normal		
Chloroform 0.24 Cc per Kg	Experiment	Preinjection	Postinjection	
			24-Hour	48 Hour
Plus choline 200 mg per Kg	{ 1	81	77	8
	{ 2	93	63	24
	{ 3	90	44	28
Plus brewers yeast 1 Gm per Kg	{ 4	79	77	40
	{ 5	84	77	10
	{ 6	87	11	< 4

N B Experiment started on third and last feeding day

This may be reconciled with the results of Miller, Ross and Whipple, Best, MacLean and Ridout, and Goldschmidt, Vais and Ravdin, on the following grounds. In the experiments of Miller, Ross and Whipple, the outstanding abnormality of their dogs was the low protein content of the plasma (and presumably of the liver). Thus the agent protecting the livers of their animals was probably the SH factor of methionine and cystine. Choline was apparently of no avail in hypoproteinemic animals against such large doses of chloroform. From Table II, of Goldschmidt, Vais and Ravdin,³⁴ it seems possible that choline did exert a definite, though small protective effect, in both experiments in which it was used (Groups 8 and 17). Both Best, and his associates, and Goldschmidt, and his coworkers, have also used relatively enormous doses of carbon tetrachloride and chloroform, respectively, as compared with the amount used in our experiments.

Methionine and cystine were compared with choline and the latter found to be more effective in normally fed dogs, although the former did show a moderate degree of protection.

		Plasma Prothrombin in Per Cent of Normal		
Chloroform 0.24 Cc per Kg	Experiment	Preinjection	Postinjection	
			24-Hour	48-Hour
Plus choline 200 mg per Kg	{ 1	100	68	41
	{ 2	91	68	70
Plus cystine 500 mg per Kg	{ 3	87	27	< 2
	{ 4	91	73	70
Plus cystine 500 mg and methionine 200 mg /Kg	{ 5	95	59	66
	{ 6	91	31	41

The exact mechanism whereby such hepatotoxic agents as chloroform and carbon tetrachloride exert their deleterious effects is not clear nor is the means whereby various factors protect against such injury entirely evident. In this connection, however, the following interesting hypothesis has been offered. The toxic agents, having reached the liver, are held there in proportion to the amount of fat present. The preponderance of central necrosis in the hepatic lobule may, perhaps, be due to the diminishing oxygen tension of the blood

and the tendency for the fats to be deposited more in this region than peripherally. The hepatotoxin then exerts its harmful effect by interfering with the normal oxidation-reduction system within the cells, involving glutathione and other SH factors. If the interference be sufficiently extensive, degeneration and necrosis result.

It is evident, therefore, that protection of the liver may be undertaken at several points. First, any factor which diminishes the exposure of the individual to the toxic agent—such as chloroform, carbon tetrachloride, phosphorus, arsphenamine, *etc*—is of vital importance in lessening the amount which reaches the liver.

Second, any factors which lower the lipid content of the liver tend to diminish the amount of the toxic agent held in the liver. Here, a high caloric diet rich in protein, and carbohydrate and low in fat is of paramount importance, the protein for its fat-displacing action and the carbohydrate largely for its protein sparing effect and to a lesser extent, perhaps, in also displacing fat. Choline, by its marked effect in decreasing the fat in the liver, is also of considerable value at this point.

Third, all factors tending to spare the oxidation-reduction system of the cells, as for example the SH group of certain amino-acids, such as cystine and methionine, may exert a protective action. Oxygen therapy is valuable in maintaining a high oxygen content of the blood circulating through the liver sinusoid and, conversely, anemia or certain anesthetic agents associated with relative anoxia may exert a deleterious effect.

Fourth, an abundance of protein is important in enhancing the regenerative phase of the liver, and here also choline and perhaps xanthine may aid by clearing fat from the injured organ.^{44 57}

Other protective actions as yet not clearly understood may result from such dietary measures, as it may be that such substances as choline and unknown B complex factors exert some specific action on the hepatic cell of which we are not as yet aware.

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DISCUSSION—DR I S RAVDIN (Philadelphia, Pa) This is a very interesting paper of Doctor Andrus and his associates, and I am very happy to discuss it The method they have used in order to improve our knowledge of the functional activity of the liver is one that is certainly in the right direction It may well be that the determination of the concentration of prothrombin and the response they have used following the intra-muscular injection, may prove to be more important from the functional point of view than any other method that is now being employed

The problem of liver protection and liver regeneration is one that must concern all of us If we think back now a period of 30 years, to the time when Opie and Alford published their historic paper on the protective action of certain foodstuffs against liver degeneration and the subsequent papers published by George Whipple and his associates, and Graham and others, we can only think of the paper published by Moses and Smith in 1924, in which they questioned the diets used by the previous investigators They pointed out that the diets which had been called carbohydrate diets were not pure diets, on the one hand, and that in many instances they were completely inadequate for growth in the animals to which they were fed

There can be no doubt that carbohydrate has protected the liver, but there can also be no doubt that carbohydrate does not offer maximum protection This statement was made 26 years ago by Dr George Whipple "Under the favorable conditions of carbohydrate diet a liver will regenerate at the rate of 100 grams of liver tissue a day"

The growth that could take place in the liver under such circumstances would have to take place from the indigenous breakdown of protein and that would be a minimum and not maximum growth

The observations my associates have been making over a period of years pointed strongly to the fact that an adequate amount of adequate protein in the diet prevents the liver from injury In the observation of Andrus and his associates, casein was not absent for a long time Three days is insufficient time Furthermore, the amount of casein in the diet must exceed 20 per cent Under such circumstances casein will protect the liver from injury It protects the liver from injury because at the present time it is the best available foodstuff to rid the liver of fat It will do it twice as rapidly as will carbohydrate Therefore, one has a minimum amount of fat in the liver after feeding period

The second relation that has been pointed out by Doctor Andrus and his associates, is the perhaps specific detoxicating factor we pointed out some years ago At that time we did not know what they were, but there is certain evidence that strong components of the protein molecule directly protect the liver

We have repeated the observations of Miller, Hawkins, and Messenger in regard to specific protective action of cystine and methionine. While cystine and methionine offer some degree of protection from a variety of these intoxications they do not offer the type of protection afforded by sterile fixation abscess with sodium arsenite or as afforded by the administration of high carbohydrate protein diet over an adequate period of time.

The problem of protection of the liver is one entirely separate from the problem of regeneration. For protection casein is the most adequate protein. In the problem of regeneration, the matter is different. There one must provide that type of protein which contains the components most readily used for regeneration and that protein is the lymph substance itself.

DR ARTHUR B MCGRAW (Grosse Pointe Mich.) I hope Doctor Andrus will forgive me for taking advantage of his paper to comment on an aspect of this immediate program that has impressed me very much and that is the part of his paper which dealt with the protection of the liver through the ingestion of casein, and furthermore, Doctor Ravdin's comments following in his discussion.

When one has been thrust rather abruptly into the Naval Service and has spent three months there one is forced very rapidly into thinking about a marked simplification of one's approach to surgical problems and also the probable necessity for compromising to some extent the methods and means which one uses in the interest of getting things done without however compromising adequacy methods or the things one has learned to know best.

These little points have come out for the protection of the liver. In the Navy we have to use chloroform below-deck we cannot use ether. We cannot very well use local or spinal anesthesia. There was a point in Dr. Moyer's paper this morning about developing antagonistic action of ether in the use of intravenous anesthesia. There were points in Doctor Siler's paper yesterday and in Doctor Brown's paper whereby we may be better able to treat the dozens of burns that may come upon us suddenly in an adequate way far better than we might be able to treat one burn by an elaborate method. These things mean a great deal to a great many people. So partly as a personal thing and partly in behalf of the Service I want to pay tribute to the helpfulness of this program which in a superficial way does not seem like a war program and also to point out that only in our type of life and point of view can these applications that can be put to war surgery come out of humanitarian surgical investigation.

DR WILLIAM D ANDRUS (closing) I have nothing in particular to say further, except to thank Doctor Ravdin and Doctor McGraw for their discussion. I did not really mean to infer that we had any doubts as to the protective action of casein. I think Doctor Ravdin and his coworkers have amply demonstrated the efficacy of that particular substance. I think it may well be that his criticism is justified and that we did not feed the animals long enough with that particular substance. We will remember that it does have a markedly protective action as was shown. I believe there were some circumstances in our animals which may have prevented the appearance of that particular action.

VITALLIUM TUBES IN BILIARY SURGERY*

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STRICTURE of the common bile duct may result from congenital atresia, ulceration from stones, or infection from septic cholangitis, but most often follows clamping, ligation, or excision of the duct during an operation for cholecystectomy. The presence of structural anomalies, the occurrence of unexpected hemorrhage deep in the wound, or the distortion of normal anatomic landmarks by infection are circumstances that may confuse even the most expert surgeon, and are likely to bewilder the operator who has not been schooled in common duct surgery.

Small strictures may be successfully treated by dilatation, division, excision, and end-to-end anastomosis, or by plastic repair to enlarge the lumen. These procedures are applicable only if normal tissue can be approximated without tension for otherwise reformation of the stricture occurs. An alternative method is by implantation of the hepatic or common duct into the stomach, duodenum, or jejunum which has the two possible faults of stricture formation at the site of the anastomosis and of ascending biliary infection from lack of the sphincter of Oddi.

Long strictures from extensive loss of the common duct create a very difficult problem which may appear insoluble when multiple operations fail to correct the defect. Three years ago such a condition was encountered in a young woman, the mother of five children, who on two occasions was asymptomatic with a rubber T-tube in the duct but who reformed a stricture shortly after its removal. This led to a trial of permanent intubation of the common duct with a Vitallium tube. The patient recovered completely and her transformation from chronic invalidism to useful living was so dramatic that it gave encouragement to try the method in others. The subject was presented⁷ at the meeting of the Society of University Surgeons a year ago. Since then more information has accumulated from animal experimentation, dissection on cadavers, and clinical experience, especially with different uses for these tubes and with modification of their design. It appears desirable at this time to report these data and evaluate the use of Vitallium tubes in biliary surgery.

COMMON DUCT STRICTURES

The first Vitallium tube was made 4 cm long, 6 Mm wide in outside diameter with a central flange 6 Mm high for an anchor which protrudes through the wall of the duct and prevents the tube from slipping out of place. No modification of the anchoring device has worked better than this simple flange and the only change that may be desirable is to shorten it to 4 Mm,

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

for sometimes it protrudes too far above the duct. Figure 1, No 1, shows in a detailed sketch how a flat piece of metal is welded to the tube to make the anchor. This flange can be grasped with a curved clamp to allow manipulation of the tube in a deep wound (Fig 1, No 2), for without this it would be difficult to insert the tube into the ends of the bile duct. Figure 1, No 3, shows how an unanchored tube may slip below the level of injury and allow reformation of a stricture. Loss of substance of the duct or fixation by scar tissue may make it difficult to bring the ends of the duct together over the tube to suture them in place. For this purpose, tension sutures pulled through the eye of the flange (Fig 1, No 4) can be used to hold the duct while doing the anastomosis. These can be removed after the suture line is completed or left in to take tension off the anastomosis if desired.

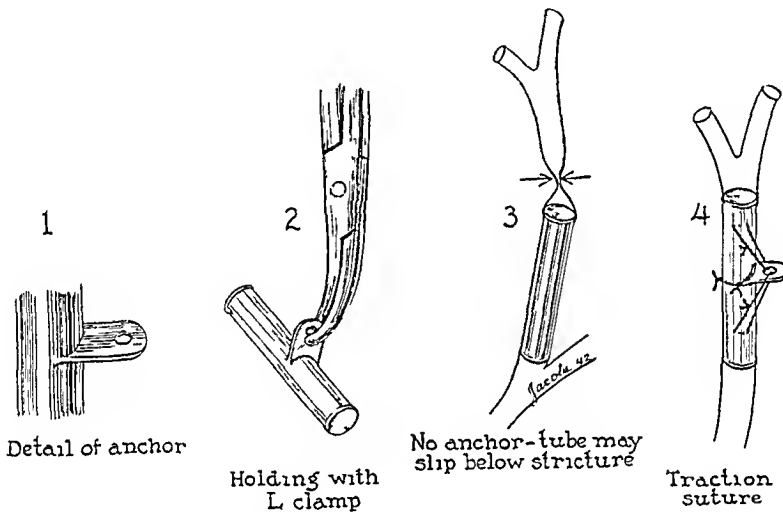


FIG 1—The flange on the Vitalium tube used to anchor it in place. (1) A detail sketch to show how a flat piece of metal is welded to the tube for an anchor. (2) Shows how the tube can be manipulated by a clamp grasping the flange. (3) A diagrammatic illustration of how an unanchored tube may slip down below a stricture allowing it to reform. (4) Demonstrates the purpose of the eye in the flange for holding tension sutures while doing the anastomosis.

The majority of the cases which require permanent intubation of the bile duct have had previous operations for repair so the ends of the duct are bound together by scar tissue. This should not be excised. The normal duct should be opened above and below the stricture and the tube inserted (Fig 2, Nos 2 and 3). In this way the Vitalium tube holds open the strictured area and there is no danger of the ends of the duct slipping off the tube. When used for this purpose it was found that the length of the tube could be shortened from 4 cm. to 3.3 cm.

The standard 6 Mm. x 3.3 cm. tube was never designed for use in anastomosing the bile duct to the intestinal tract, in fact it was created to avoid that very thing and so preserve the function of the sphincter of Oddi. However it has been used by others on several occasions for hepaticoduodenostomy (Fig 2, No 4), apparently to prevent stricture of the anastomosis. This is the only possible advantage of such use and even this may be vitiated

by the tendency of all tubes used in this way to pass into the gastro-intestinal tract

Loss of part of the duct followed by infection and scar may leave the two ends fixed in widely separated positions. Attempts to bridge this gap by a Vitallium tube tied into each end of the duct have failed because of retraction of the duct off the ends of the tube. To overcome this, a straight tube 6 cm long was made but it was so awkward to use that it was discarded. Perhaps a long tube bent in the center to accommodate the angulation of the ducts would work better, but this condition has been successfully treated in another way. The stump of the common hepatic duct is dissected free in the sulcus

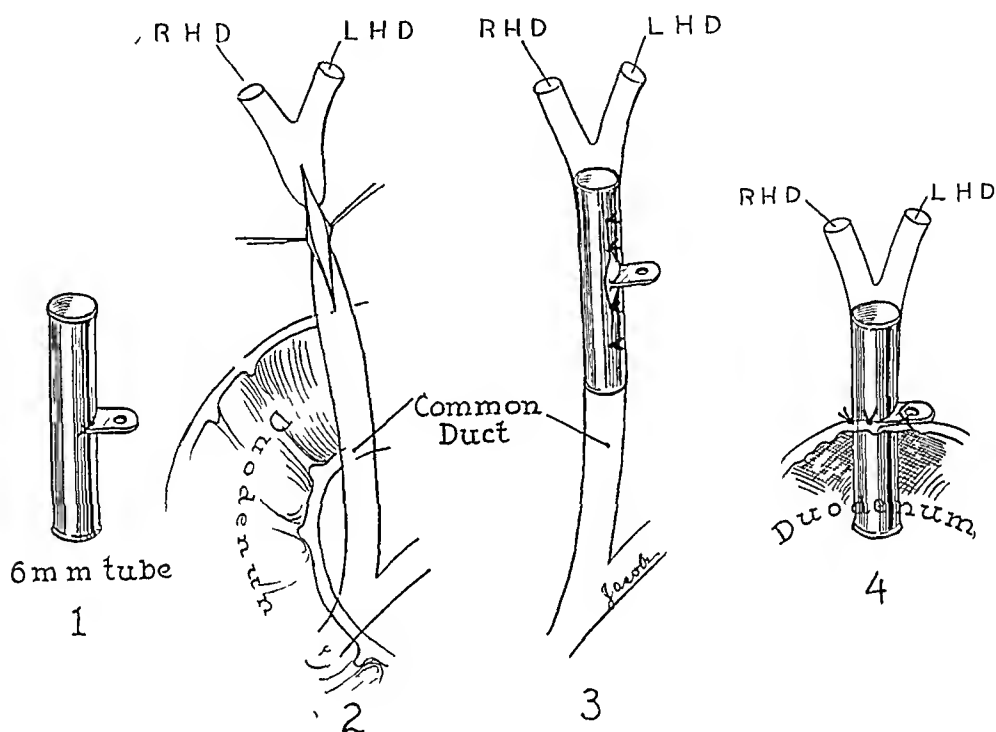


FIG. 2—(1) The straight tube 33 cm x 6 mm (2) For holding open a strictured area the tube is slipped into the duct, which is then closed over it, leaving the anchor flange protruding through the suture line (3) (4) The use of this tube in hepaticoduodenostomy

transversus of the liver and the common duct is searched for by freeing all tissue off the hepatic artery and portal vein. If it is not found, the duodenum is rolled out and down and the scar tissue beneath it carefully dissected and sectioned. In this way the common duct is usually found underneath the duodenum and so closely attached to it that it appears to be a part of the bowel wall. At this stage the gap may look to be irreparable but after both ends of the duct have been completely mobilized they can be brought together by pushing up on the duodenum and pancreas and pulling on the ends of the duct. End-to-end anastomosis under these circumstances is done under tension, and a stricture will usually form, so this is prevented by doing the anastomosis over a Vitallium tube. Another successful method is to use a rubber T-tube until all infection subsides and after two months reoperate upon the patient, remove the T-tube and insert a Vitallium tube.

COMMON HEPATIC DUCT STRICTURES

The anatomic nomenclature calls the common hepatic duct that part between the bifurcation of the right and left hepatic ducts and the junction of the cystic duct. That below the cystic duct is called the common bile duct. The studies of Nuboer⁶ have shown that because of the anomalies of the cystic duct the common hepatic duct may vary from 0 to 5.8 cm in length and the common bile duct from 3 to 9.5 cm in length. Surgeons often speak of the common bile duct as that part which is exposed below the liver in the gastro-hepatic omentum. This is logical, for treatment of this part is the same irrespective of the relation of the cystic duct. On the other hand, injury, or stricture, within 1 cm of the bifurcation of the hepatic ducts creates distinct problems of management which are not present at a lower level. For the purpose of this discussion, these will be called common hepatic duct injuries or strictures.

Dr Howard M. Clute first succeeded in curing a patient with only about one-eighth inch of common hepatic duct remaining after four unsuccessful operations. A Vitallium tube with a trumpet-shaped end (Fig 3) was designed and inserted into the stump of the common hepatic duct so that it would act as a funnel for the bile from the right and left hepatic ducts. The lower end was placed in the common duct and an anastomosis done over the tube.

Some of the situations encountered in these high strictures of the common hepatic duct are shown in Figure 4. A complete external or internal fistula leading from the common hepatic duct (Fig 4, No 1) is usually associated with a closed functionless common duct which must be sought in scar tissue without any tract as a guide to it. The common hepatic duct has been found to empty into a bile-filled cavity (Fig 4, No 2) which communicated with an external fistula and

FIG 3—The trumpet shaped tube used by Clute for a high stricture of the common hepatic duct is shown in a postoperative roentgenogram taken with barium filling the stomach.

the common duct. Nature may attempt to reconstruct the injured area by a long, narrow, constricted passage (Fig 4, No 3) through scar tissue. This channel may be no bigger than a string and yet carry enough bile to prevent severe jaundice.

Much thought has been given to the design of tubes for use in the hepatic duct strictures. The anteroposterior curvature of the ducts, the bifurcation

of the hepatic ducts so near the end of the common hepatic duct and the inaccessibility of these structures in the sulcus transversus of the liver create problems in technic that are difficult to overcome. The trumpet-shaped end of the tube (Fig 4, No 4) used by Clute does not enter either of the primary

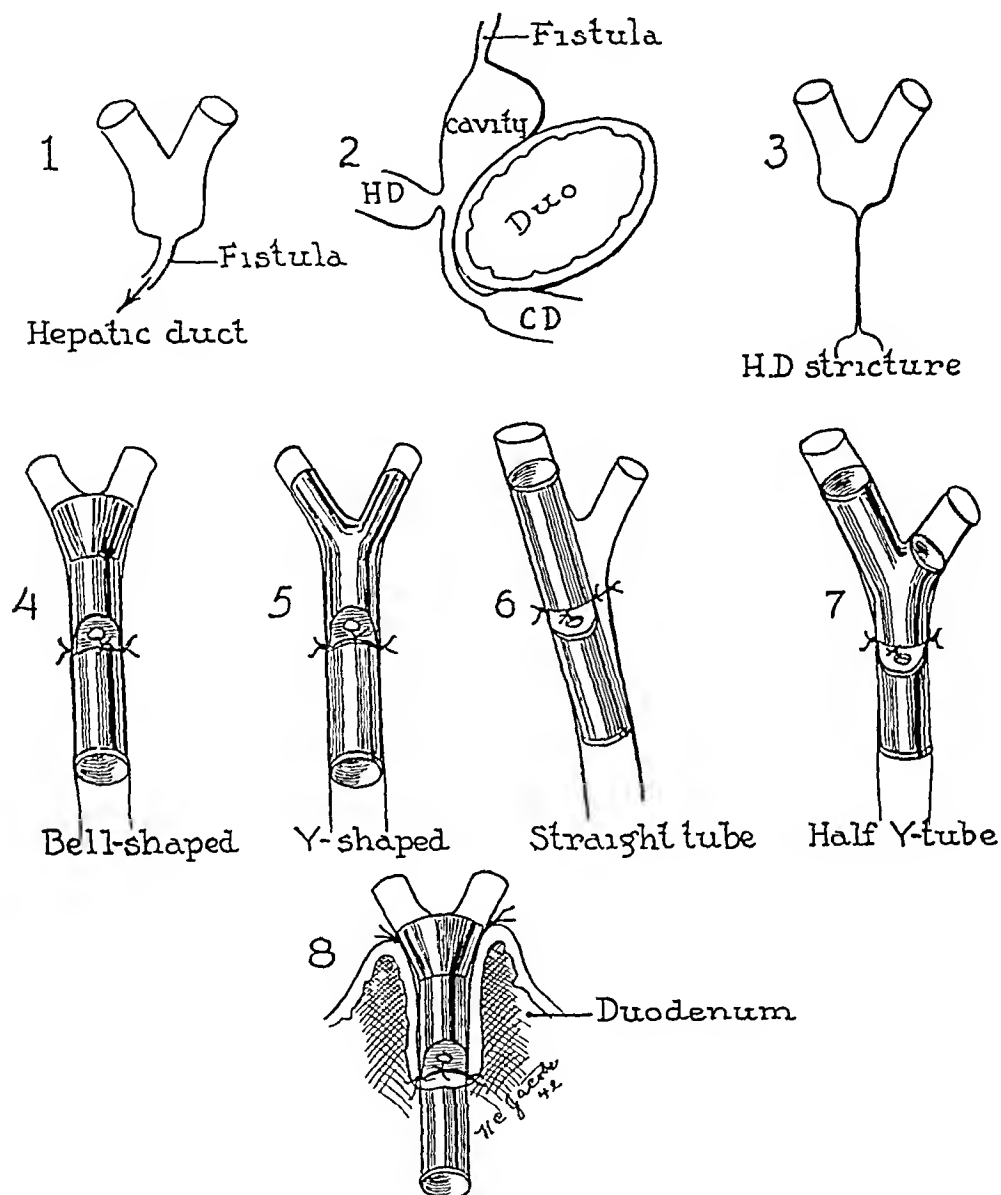


FIG 4—The conditions found in strictures of the upper common hepatic duct may include an external fistula (1) associated with a functionless common bile duct, a communication with a bile filled cavity (2) which drains into a fistula and the common duct or, as in (3) a long threadlike channel joining the ends of the ducts.

In 4, 5, 6, and 7, are illustrated the tubes that have been used in high strictures of the common hepatic duct. Here, the inaccessible bifurcation of the hepatic ducts close to the stricture in a short stump of the common hepatic duct creates mechanical problems of management. Zininger used the bell or trumpet shaped tube for hepaticoduodenostomy (8) when the end of the common duct could not be found.

hepatic ducts so has little to hold it in place. If it is unstable and slips away from the hepatic ducts, it may not drain their bile. To overcome this, a Y-shaped tube (Fig 4, No 5) was made with 4 Mm openings at the two proximal ends. Even so, the distance across the two limbs of the Y is 1.3 cm, in contrast to the 1 cm width of the funnel on the trumpet-shaped tube. The right and left hepatic ducts meet at an angle which varies between 80° and

90°, so the limbs of the Y cannot be brought much closer than this, yet it is difficult to insert them through the stump of the common hepatic duct when they are this far apart. If the hepatic ducts are not too deeply buried in the liver, one or the other can be visualized and slit up the outer side to give room for inserting the Y-tube. In one patient neither the trumpet-shaped nor Y-tube could be inserted so a straight 6 Mm tube was put up the right hepatic duct (Fig 4, No 6) for want of anything better to do. After operation the

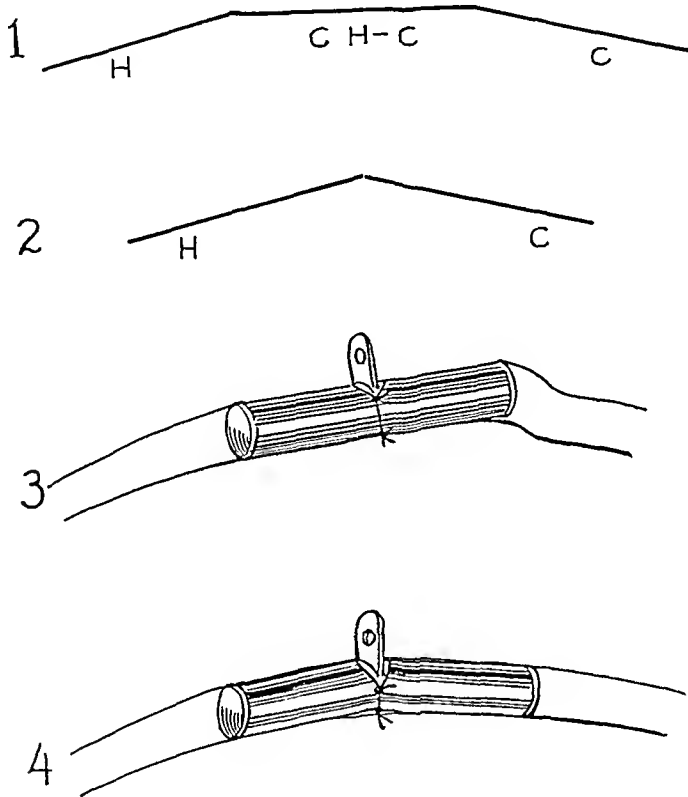


FIG 5—(1) The diagrammatic representation of the angulation of the ducts where the hepatic ducts have an anterior inclination, the distal common duct a posterior declination, and the central part of the common hepatic and common bile ducts and horizontal. If this middle part is destroyed (2) then the upper and lower part of the ducts come together at an obtuse angle of about 170°. This causes a straight tube to tip up at one end (3), and may cause pressure necrosis or kinking of the duct. To avoid this a tube has been designed with a bend forming a 170° angle, which will be most useful in the high common hepatic duct strictures.

left lobe of the liver enlarged, then shrunk and though it may become cirrhotic, yet the patient is well without any signs of hepatic insufficiency. This led to the design of the tube shown in Fig 4, No 7, which is essentially a half Y for one limb is cut off. Instead of this, one might have only a hole on the left side so the bile from the left hepatic duct could get into the tube, but unless this opening was accurately placed over the orifice of the duct it would not serve its purpose. Exact placement might be difficult to do by sense of touch so it was thought desirable to have a short stub on the left side to indicate when it was in the correct position. Zinninger¹⁰ describes the anastomosis, shown in Fig 4, No 8, in a case where no remnant of the common

bile duct could be found. The trumpet-shaped tube was used for hepatico-duodenostomy and this anastomosis secured by rolling the duodenal wall up onto the hepatic ducts.

A straight tube inserted into the hepatic ducts above and the common duct below tends to tilt up at one or the other end. This is due to the slight anterior inclination of the hepatic ducts and the posterior direction of the common duct which is shown in Figure 5. The diagram in Figure 5, No. 1, shows the central part of the common hepatic and common ducts to be horizontal. If this is destroyed so that the proximal hepatic duct is joined to the distal common duct, an obtuse angle is formed. No information could be found in the literature on this,¹ but measurements taken at operation and on the cadaver showed this angle to be about 170° , or a deviation of 10° from

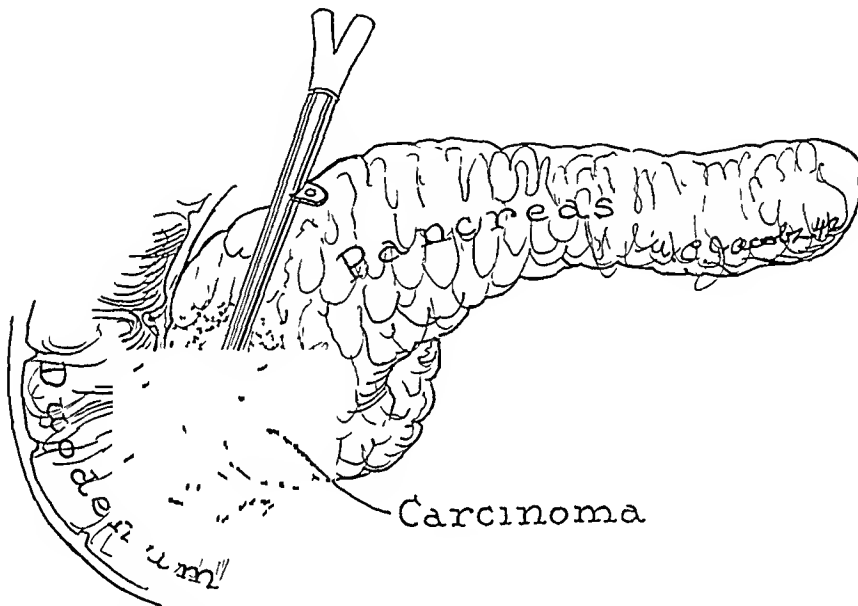


FIG. 6.—An 8 cm tube which tapers from 6 to 4 mm in diameter is illustrated. For use in the palliative treatment of occlusion of the bile duct from carcinoma. This might be used instead of cholecystogastrostomy.

the horizontal. To prevent the tilting of the straight tube shown in Figure 5, No. 3, efforts were made to manufacture a curved tube. Vitallium is a very hard alloy which cannot be bent, molded, or machined but must be cast. Curving the tube prevented polishing it around the bend on the inside, so finally the manufacturer suggested welding two pieces of straight tubing together at an angle of 170° , as shown in Figure 5, No. 4. It is expected that all tubes designed for treating strictures of the proximal common hepatic duct will have this anteroposterior angulation. But this raises the question of where to put the bend, for it should come at the site of the anastomosis yet the stump of the common hepatic duct may be as short as 3 or 4 mm or as long as 1.5 cm in different cases. The bifurcation of the hepatic ducts fixes the position of the tube above and the length of the common hepatic duct determines the location of the anchor flange and bend below. A rigid tube cannot be altered to conform to the different distances between these points in different cases so an average length will have to be used. It would appear

¹ I find that Dr. D. B. Pheiffer of Philadelphia has described this angulation.

that a length of 1 cm from the lower part of the bifurcation of the tube to the bend and anchor would meet the needs of most cases

MALIGNANT STRICTURES

Vitallium tubes have been considered for use in the palliative treatment of malignant occlusion of the bile ducts. The only one that has been made was intended for obstruction from carcinoma of the head of the pancreas. This tube was made 8 cm long for the average combined length of the common hepatic duct (3.3 cm) and the common bile duct (6.3 cm) is 9.6 cm. The tube need not go far up into the common hepatic duct so a length of 8 cm should permit intubation of the duct into the duodenum. The anchor flange was placed 2 cm from the upper end where the diameter of the tube is 6 mm. From this point the tube tapers to 4 mm (Fig 6) to allow insertion through a carcinomatous stricture.

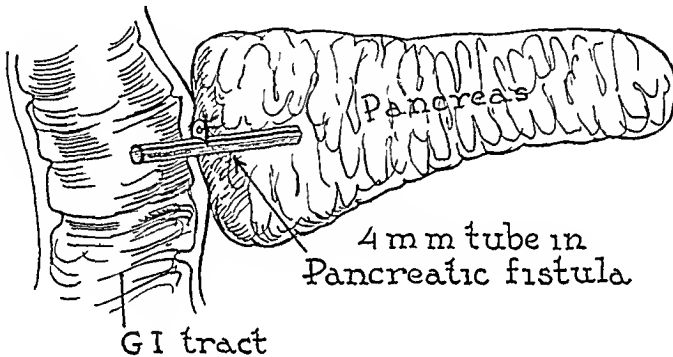


FIG 7—A 4 mm Vitallium tube is shown inserted into the pancreatic duct for repair of a pancreatic fistula following resection of the head of the pancreas for carcinoma. This method, used successfully by Zininger, suggests the need of tubes with one short end for implantation into the gastro intestinal tract.

PANCREATIC FISTULA

A straight Vitallium tube, 4 mm in diameter, has been used to close an external pancreatic fistula. The case report sent to me by Zininger¹⁰ is as follows:

Case Report—A male, age 62, presented signs, symptoms, and laboratory findings of complete obstructive jaundice from periampullary carcinoma. On October 31, 1939, a first-stage modified Whipple operation was performed. On December 9, 1939, the duodenum and the head of the pancreas were resected for adenocarcinoma of the ampulla of Vater. A pancreatic fistula developed. Every time the fistula closed the patient developed chills and fever, and the fistula had to be reopened. On May 1, 1941, the fistula was traced to the pancreatic stump, one end of the Vitallium tube was inserted into the pancreatic duct (Fig 7) and the other end implanted into the stomach. The patient's general condition promptly improved. The wound healed by May 19, 1941, and has remained healed ever since.

The use of Vitallium tubes has been thought of in connection with the treatment of some types of hydrocephalus, the repair of ureteral and urethral strictures, and the reconstruction of the vas deferens and fallopian tubes but they have never been reported as used for these purposes.

Discussion—The question is often asked, what reaction will be caused in the tissues by the presence of Vitallium tubes? Thus far, there is information from only one human case obtained by reoperation, where it was found that little or no reactive inflammation existed. Additional data was sought by means of animal experimentation. Vitallium tubes placed in the common bile duct of dogs remained patent without erosion of the metal or deposition of pigment or salts on them. Most important of all was the absence of reactive change in the mucosa lining of the duct for this would indicate good tolerance of the tissues to the metal. A section of one of these ducts was illustrated in a previous paper.⁷ The mucosa was never found to grow inside the tube so one must depend upon the bare metal for the conduction of the bile. Vitallium is an alloy of cobalt, chromium, and molybdenum which has been found to be inert in bone,^{8, 9} joints,⁴ and the brain^{1, 3} so the absence of reaction in the bile ducts is not surprising.

A review of the various methods of treating injuries or strictures of the bile ducts is not presented, for this audience is already familiar with them and the reviews of Kehr⁵ and Eliot² have discussed them in detail. It is expected that Vitallium tubes will only be used in biliary surgery where extensive damage has occurred and where other methods have failed, for otherwise their indiscriminate use may result in disappointment or even discredit of the method.

SUMMARY

(1) Injury to the bile ducts which was irreparable by other methods has been successfully treated by the permanent implantation of a Vitallium tube.

(2) A straight 3.3 cm x 6 Mm tube with a central flange to anchor it in place is most useful to hold open a strictured area of the common bile duct.

(3) Loss of a part of the common duct is best repaired by approximating the ends over a Vitallium tube even if tension must be used. This will hold the ends of the duct together and the tube will prevent occlusion by stricture. It may be dangerous to bridge a gap by tying the tube into the ends of the duct for it may slip out of place.

(4) Injury or stricture of the common hepatic duct within 1 cm of the bifurcation of the hepatic ducts produces mechanical problems that require special designs to meet them. For this purpose tubes with trumpet-, Y-, and half Y-shaped ends have been made.

(5) Vitallium tubes have been used for the repair of a pancreatic fistula and one has been designed for the palliative intubation of malignant occlusion of the bile ducts. Other uses for these tubes such as in the brain and genitourinary tract have been considered.

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DISCUSSION—DR HOWARD M CLUTE (Boston, Mass) I think Doctor Pearse's work marks a new step a new era if you like in the management of bile duct strictures which we all know have been one of the most difficult problems which have faced surgeons and I think it also is significant because it shows us that in the cavity of the body we may put in this metal and have it stay there for a long time without any material change in the viscus in which it lies It opens possibilities perhaps for the use of Vitallium in many places in the body other than the common bile duct

For example in my hospital the urologist has used a Vitallium tube in the perineal urethra, which constantly strictured following amputation of the penis, and he has been able to have a Vitallium tube fitted into that—which has been used successfully and satisfactorily

The laryngologist has had a mold made to use in the stricture of the larynx which he was trying to treat with skin grafts and hopes to overcome the stricture

My personal experience with Vitallium tubes is limited to a case conducted by my associate, Doctor Albright about two weeks ago in which I helped

There is another case of a friend of mine that I advised Doctor Hedisheimer of New Bedford Doctor Hedisheimer's case has gone on for some five months now Doctor Albright's is very recent

Then there is the other case that Doctor Pearse mentioned the case I cared for myself I would like to show the lantern slides of that if I may This lady had had four previous operations starting with her original cholecystectomy and injury to the common duct and three other operations to repair this two of which I had performed the fourth operation the last one that I did being a cholecystohepaticoduodenostomy In six or eight months this failed to function any further and we finally reoperated upon her for the fifth time after learning from Doctor Pearse of these tubes

This is more or less the picture that we found after we had separated the duodenum from the common duct We found complete absence of the common duct in this area The picture does not show it but we catheterized the common duct through the ampulla of Vater and that helped in finding this at the distal end, which by no means is as clear as the artist has drawn

The tube we used was a funnel-shaped affair which we had made because we knew from three previous excursions into this area that this stricture was deeply into the liver and we would have a very difficult time to hold anything in it The funnel-shaped tube was then put in the liver the other end over here The surrounding tissue was laid around it as well as we could Silk sutures were put here in this very dense fiber that remained in the common hepatic duct I think it was good fortune that in the 16 months past since this operation the tube has not slipped out However it is to be noted it seems to me that in this case we had a gap larger than the artist shows in my recollection three-quarters of an inch in which there was no common bile duct at all If the gap had not been here I agree with Doctor Pearse that it would have been very much to our advantage to approximate the ends and this no doubt could have been done if one freed the duodenum and freed the hepatic duct

This is a slide similar to the one Doctor Pearse showed you but taken some six months after the operation when the patient had an attack of pain and a slight jaundice

and I was afraid that something had happened but it cleared up in a matter of two days We took this picture just to see whether the tube was where it should be, and it was

The last slide shows the various tubes I got from Doctor Pearse and some we had, for your observation of the types that have been made Doctor Pearse has enlarged on these since then Though it is apparent that this tube can be used to replace absent common duct and that it will last for a long time and I believe from this case at least that you can have the common duct absent over quite a distance and not pull the two ends of the duct together, as Doctor Pearse recommends and as we recommend, and still have it go on there is more danger of course that the tube may fall out

I think there is a great advantage and it is to be emphasized, that you should have the distal end of the common duct toward the distal end of the tube if possible, as Doctor Pearse has said because in that way you preserve the sphincter of Oddi, and which is of great advantage In fact, I think it is of such advantage that in Doctor Albright's case I could not find the distal duct and urged him to open the duodenum and find it from within and having opened the duodenum we found it

It seems to me that these tubes can be used in biliary strictures of certain kinds Certainly, I believe they have an advantage over any such procedure as transplantation of external biliary fistula which carries such a high percentage of failures I think they are preferable to rubber tubes even with the slight knowledge we have, and are very valuable when one can use them with the preservation of the sphincter of Oddi, as in these instances

DR EUGENE W ROCKEY (Portland Ore) Not knowing of Doctor Pearse's work, some three years ago, I attempted a somewhat similar series of experiments on dogs using several different substances, and finally settled on metallic magnesium I found that with those dogs there was no irritation of the gallbladder wall when the tube was implanted into it and that I got the tubes of the thickness so that they would last from eight to 12 weeks There was no bile deposited in these tubes

I then implanted such tubes in two humans The tube did not have the advantage of the lateral flange which Doctor Pearse had and in one case the tube slipped down into the duodenum That was an implantation in the duodenum

I was about to publish this experience and got a new lot of metallic magnesium tubes from the Dow Chemical Company I planted those in the dogs gallbladders and had the misfortune to find that bile salts were deposited on the tubes, which had not been the case originally I sent the magnesium back to have it analyzed and find whether it was pure magnesium or had some alloy in it which was irritating

The Vitallium tube apparently has a distinct advantage over the metallic magnesium which I have been using, but I am sure there is a very great need for such a bridge for a stricture of the biliary duct

DR WALTER G MADDOCK (Ann Arbor, Mich) About a year ago, I first heard of Doctor Pearse's work with the use of this tube, and he supplied two for us to use I have had the opportunity of trying them on two patients

The first one about 11 months ago, came in with a history of multiple previous operations for obstruction to the common duct This patient had a T-tube in place, and I simply took the T-tube out and slipped the Vitallium tube into the site of it, and it seemed to fit nicely in that direction and did not move up and down This patient has gone ten months without any difficulty as far as the obstruction is concerned During the past month however she has begun to have attacks of chills and fever and jaundice It may be that she will get over it, as Doctor Clute's case did but I am much concerned about the situation, and I feel that something subsequent may be necessary

A month ago I had a chance to use the tube again on a much similar case, with previous history of operations upon the common duct because of stricture occurring post-operatively At this time a rubber T-tube was in place The common duct was cleared downward, but the approach to the hepatic ducts was not as wide-open as I would have liked it I could not get a uterine sound up that section very well A small probe, however did pass The patient had requested however, to dispense with the rubber tube, if possible, so I slipped one of these Vitallium tubes into place with-

out disturbing the site of it very much That patient has not done well She is having chills and fever and has had intermittent jaundice on two occasions

I think this is just an addition to the experience with these Vitallium tubes, and fear that my two cases are going to require some further type of treatment I do not know what it is going to be

DR LEO ELOESSER (San Francisco, Calif) Just two short points of technic In a man who had had a very complicated history including fistula between his transverse colon and his gallbladder a bleeding duodenal ulcer, and several other complications, an obstructive biliary cirrhosis ensued with an intermittent obstruction, sometimes on his right and sometimes on his left In the first attempt to overcome this obstruction, finding a very tight duodenum and having had a bleeding ulcer to deal with, we did a hepaticoduodenostomy and anastomosed the open stump of the duodenum to the hepatic junction That gave a very wide union between the hepatic junction and duodenum, but the wide union still was not sufficient to overcome the strictures which reformed in the hepatic duct

I used one of Doctor Pearse's tubes and slipped it into the right duct, but I was confronted with the same situation that he delineated on the second line of his third slide, I think the last one to the left in which there was a little button projecting, as it were as a flange from the side of the tube because the situation of the duct was such that it would have been quite impossible to introduce a Y-shaped tube I questioned in that case whether it would be feasible although I had none at hand to make a tube with a clip joint as it were so that it would be possible to introduce one branch of the Y and then snap the other branch Y into the other hand of the hepatic ducts

The patient, to whom I refer died five days after his operation of secondary rupture of his wound and pneumonia We obtained the specimen and the tube was in place There was no effect of the tube on the surrounding tissues and no erosion and the tissues were perfect in reaction

DR HERMAN E PEARSE (closing) One word about bridging the gap We have attempted to do this by a longer tube long enough to prevent the ducts retracting off The disadvantage was the tilting of the tube and when a straight tube 6 cm long, was made it was too awkward to be of any use Now that we have a method of making an angulated tube it may be possible to devise one long enough to bridge an extensive gap

I was very much interested in Doctor Rockey's comments because I am at present contemplating some experiments with Dow metal for an entirely different purpose Men who have been wounded in aircraft combat who had fragments of magnesium in their tissues have been found to develop an extreme fibroplasia about metallic magnesium so much so that Doctor Walters has been able experimentally, to shut off the ureter by encircling it with a clip of Dow metal I was interested in this as another possible means of gradually occluding large arteries by fibroplasia

It is interesting that magnesium in the biliary system did not produce this fibroplastic reaction

Of the two patients mentioned by Doctor Maddock the latter one might well be reoperated upon, perhaps with the insertion of a tube above the hepatic stricture We have had one instance of recurrent chills fever and jaundice in a patient one year after intubation, in which we suspected occlusion of the tube from cholesterol We gave her sodium taurocholate and these symptoms disappeared

Also, one must remember that these patients have had a long history of liver infection and some of their postoperative difficulty may be due to hepatitis

SPONTANEOUS INTERNAL BILIARY FISTULA*

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FISTULAE between some portion of the biliary tract and some hollow viscus have been known to exist for many years. Pathologists have described fistulous communications between the gallbladder or bile ducts and nearly all portions of the gastro-intestinal tract as well as with the bladder, uterus, kidney pelvis, portal vein, ovarian cysts, and with such intrathoracic structures as the pericardium and bronchial tree. In an excellent literature review and survey of their own material, Borman and Rigler record the presence of only 67 internal biliary fistulae in over 30,000 autopsies. Many such passages undoubtedly were overlooked because intestinal obstruction due to gallstones was mentioned in the early literature three times as frequently as gallbladder intestinal fistula.⁴ Undoubtedly most gallstones sufficiently large to produce obstruction have reached the lumen of the bowel through a fistula.

With the more frequent recognition of internal biliary fistulae in the operating room and their frequent roentgenologic diagnosis, clinical interest in this condition has increased. Kehrer reported the finding of 100 biliary fistulae in 2,000 cholecystectomies, an incidence of 5 per cent. Bernhard encountered them 109 times in 6,263 operations upon the biliary tract. At the University Hospitals of Iowa 12 per cent of all patients with cholecystitis were found to have internal biliary fistulae.⁵ Judd and Burden reported 153 fistulous connections between the biliary and gastro-intestinal tracts. The great majority of these were not diagnosed before operation. In Judd and Burden's series only two were diagnosed preoperatively, one of which was visualized roentgenographically.

Roentgenographic diagnosis of internal biliary fistula is based chiefly upon the presence of air in the biliary passages or the influx of barium during a gastro-intestinal study. The passage of barium was noted first by Hunt and Herbst in 1915. During the following ten years many reports have been made of roentgenographic recognition of internal biliary fistulae. Borman and Rigler collected all reports to 1937 which totaled as follows:

Cholecystoduodenal	31
Choledochoduodenal	16
Cholecystocolic	10
Cholecystogastric	3
Cholecystoduodenocolic	1
Cholecystojejunal	1
Choledochocolic	1
Biliary-bronchial	4

They also listed 16 instances of regurgitation of barium into the common duct. In spite of the increased interest in and recognition of such fistulae by

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

roentgenologists, it is probable that only a small percentage of them are diagnosed prior to operation. This is due largely to the small numbers of such patients upon whom gastro-intestinal roentgenologic studies are made.

Most internal biliary fistulae are formed by the erosion of a gallstone through the wall of the gallbladder or common duct into an adjacent viscus. Obstruction of the ducts below the stone is usual and a severe inflammation is thought to accompany the process. Duodenal ulcers are believed occasionally to invade the adjacent wall of the gallbladder and produce a fistula. Malignant lesions also are considered as etiologic factors.

In a series of 500 operations for benign biliary tract diseases I have encountered spontaneous internal biliary fistulae in 16 patients, distributed as follows:

Cholecystoduodenal	9
Cholecystoduodenal and cholecystocolic	1
Cholecystocolic	2
Cholecystogastric	1
Cholecystocholedochal	1
Hepaticoduodenal	1
Hepatobronchial	1

SYMPTOMATOLOGY

It frequently is stated that patients who develop spontaneous internal biliary fistulae give a very longstanding history of gallbladder disease, often severe, with colics, fever, and jaundice, and then after a particularly severe attack are relieved of all of their symptoms. It is thought that the formation of the fistula is followed by a relief of distress. Such has not been true in this series.

The duration of symptoms varied from one month to 27 years. Four patients had symptoms for less than one year and four others for less than four years. The average duration of symptoms for the group was eight years in comparison to six years for the entire group of patients with biliary disease. Moderately severe to intense colics were complained of by all patients. All but four patients complained of fever, usually accompanied by chills. Recurrent or fluctuating but persistent jaundice occurred in 11 of the 15 patients with intra-abdominal fistula. The majority of these patients were acutely ill, debilitated, and many lost from 20 to as much as 80 pounds in weight. In no case was intestinal obstruction present due to stone but one patient had marked duodenal obstruction due to pressure of the distended gallbladder and cicatricial stenosis at the site of a cholecystoduodenal fistula. The majority of these patients were much sicker and had more severe symptoms than usually are seen in cholelithiasis. In most instances there was a steady progression of symptoms and in none was the history suggestive of relief of symptoms coincident with the formation of an internal fistula.

In this group of 16 patients, preoperative roentgenographic diagnoses were made in two cases. In one with a cholecystoduodenal fistula the gallbladder filled with barium (Fig. 1) during a gastro-intestinal study. Several days later many of the intrahepatic bile ducts had become filled with gas and

were outlined on roentgenograms (Fig 2) A barium meal administered to the other patient revealed a cholecystogastric fistula This case is discussed later in detail Two other patients at the Illinois Research and Educational Hospitals have had roentgenographic diagnoses of internal biliary fistulae one patient whose roentgenograms revealed a cholecystoduodenal

FIG 1

FIG 2

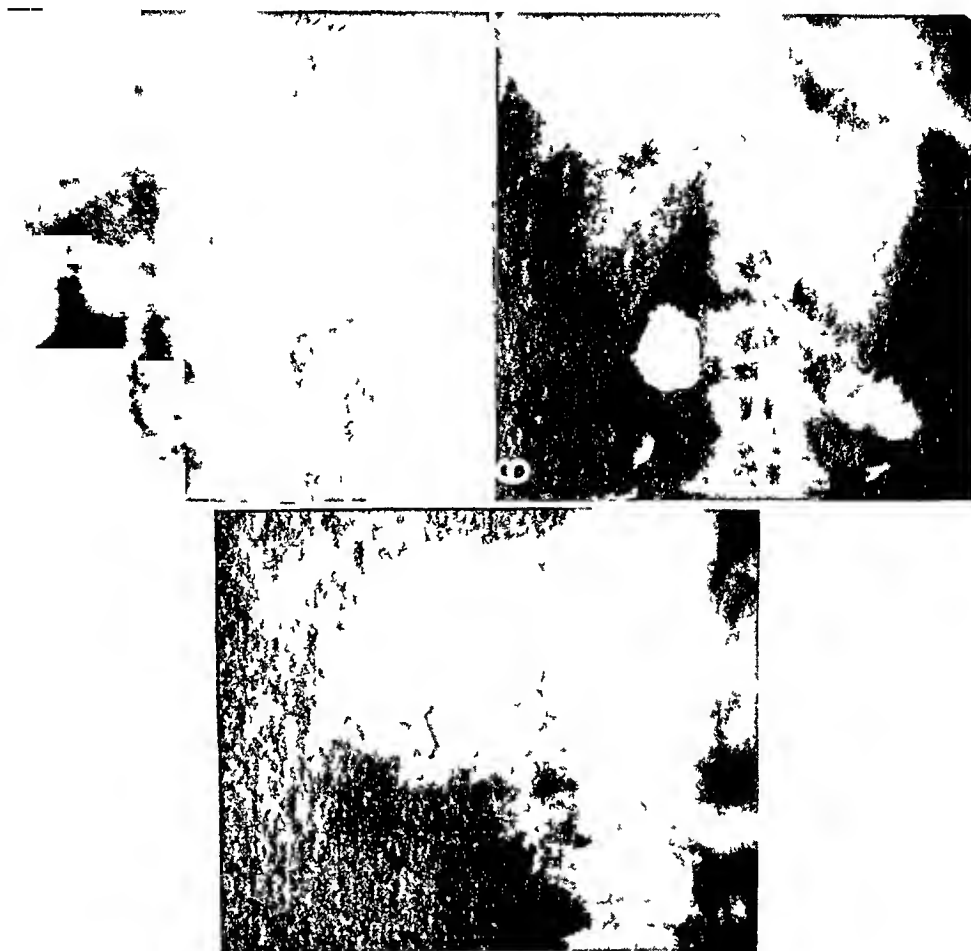


FIG 3

FIG 1 —Cholecystoduodenal fistula Gallbladder filled with barium
FIG 2 —Same patient as Figure 1 Film taken some time later revealing gas through out gallbladder and bile ducts
FIG 3 —Regurgitation of barium through choledochoduodenal fistula visualizing bile ducts, gallbladder, and one large stone in the choledochus

fistula refused to be operated upon Roentgenograms of the other patient revealed a choledochoduodenal fistula (Fig 3) She was operated upon by Doctor Warren H Cole, who found an opening between the common duct and the superior margin of the duodenum, evidently produced by the erosion and passage of a stone Other stones were found in the common duct

OPERATIVE FINDINGS AND PROCEDURES

Seven of the nine patients with cholecystoduodenal fistulae gave a history of jaundice All seven had one or more large stones present in the common duct One of the two patients without a history of jaundice had an obliterated cystic duct The fistula into the gallbladder was large and patent and the

gallbladder was badly diseased. The common duct was not enlarged or diseased and did not contain stones. Evidently this patient developed a cystic duct obstruction before the fistula was formed and the bile ducts were not subjected to contamination by regurgitated intestinal contents. The other patient without a history of jaundice had been operated upon 18 years previously and was of the opinion that her gallbladder had been removed. After frequent attacks of epigastric pain for many years she finally developed symptoms of duodenal obstruction. A diagnosis of an obstructing duodenal ulcer was made. At operation the gallbladder was present and filled with stones. The cystic duct was very small and the common duct appeared normal. A patent fistula existed between the gallbladder and duodenum with marked stenosis of the intestine. Cholecystectomy was performed and the duodenum closed but as the lumen of the bowel was very small, a posterior gastro-enterostomy was made.

One male patient, aged 42, gave a history of biliary colics with jaundice for 17 years. Four years before coming under our care a cholecystostomy had been performed. Attacks of pain, fever, and jaundice occurred a few days after operation and recurred at frequent intervals. He became progressively more emaciated and more frequently jaundiced. For six weeks prior to our first operation he had constant chills, fever, and jaundice. A patent cholecystoduodenal fistula was taken down and the duodenum closed. Extensive edema and infection were present throughout the entire extrahepatic biliary tract. The common duct was greatly dilated, thickened, and contained "white bile," many large and small stones with much sand and pus. The gallbladder was filled with stones and was removed. The common duct was emptied and drained with a T-tube. The patient recovered and was well for six months when he again developed colics and jaundice. The common duct was reexplored and found to be filled with stones. These evidently had formed since the last operation. The inflammatory changes in the ducts noted at the previous operation had greatly subsided. All stones found were removed and the duct again drained for a month. The patient remained well for six years when he again had mild attacks of biliary colic with transitory jaundice but without fever. A third exploration of the common duct revealed one stone at the distal end. All evidence of infection in the duct wall had disappeared. He has been free of symptoms since this operation.

The patient with both cholecystoduodenal and cholecystocolic fistulae had been jaundiced. After dividing the fistulae and closing the stomata in the colon and duodenum, exploration revealed marked infection of the gallbladder with edema and inflammation throughout the gastrohepatic omentum and inflammatory lymphadenitis. Because of this, only a partial cholecystectomy was performed and the common duct was not explored.

Both patients with cholecystocolic fistulae had persistent right upper abdominal pain and tenderness associated with fever for several weeks. Neither had been jaundiced. At operation one patient had an extensive inflammatory mass and in attempting to isolate the gallbladder a large cholecystocolic fistula

was separated. The large opening in an acutely inflamed hepatic flexure of the colon was closed with difficulty. The gallbladder was removed but the common duct was not exposed because of the extensive edema and inflammation. The second patient likewise had marked swelling and acute inflammation of the gallbladder and bile ducts. After taking down the fistula and closing

FIG 4



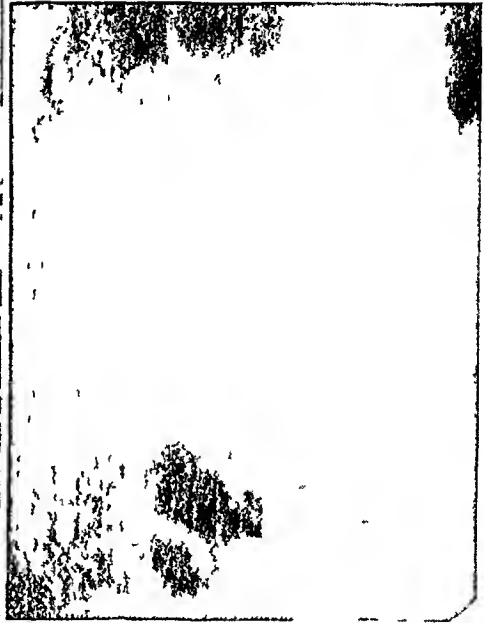
FIG 5

FIG 4—Barium has passed through a cholecystogastric fistula outlining gallbladder and both extra and intrahepatic bile ducts. Calculi can be seen displacing barium in gall bladder and in the distal end of the choledochus.

FIG 5—Film taken 24 hours after Figure 4. Considerable barium is still present in the intrahepatic ducts.

FIG 6—Same as Figure 4. Film taken six days after administration of barium showing that most of the barium had passed out of the liver through the fistula.

FIG 6



the colon, it was thought safer to remove only a portion of the gallbladder. The virulence and acuteness of infection in the gallbladder and bile ducts was much more marked when cholecystocolic fistulae existed than when the gallbladder communicated with the duodenum.

Cholecystogastric fistulae are much less frequently found than cholecystoduodenal stomata because of the less frequent anatomical proximity. Three

previous cases have been diagnosed by roentgenograms³ Because of a number of interesting features of our case, a brief abstract of the history is given

CASE REPORTS

Case 1—R, male, age 62, had no symptoms referable to the gastro-intestinal tract until six months prior to the time of operation. During this time he complained of qualitative food distress manifested by bloating and belching. Two weeks before admission to the hospital he noted midepigastria distress and the onset of a gradually increasing jaundice. A week later he had his first chill with a fever of 102° F. Upon admission to the hospital a barium meal revealed a cholecystogastric fistula and visualized the intrahepatic bile ducts (Figs 4, 5 and 6). A stone could also be seen blocking the lower end of the choledochus. For three weeks chills and fever recurred almost daily. The passage of barium into and out of the liver and the presence of bile in the duodenal contents indicated that the fistula was patent. The icterus index remained at 60. At this stage the patient evidently was suffering from a severe cholangitis and hepatitis induced by the reflux of intestinal contents into the bile ducts and his jaundice was intrahepatic in type (Chart 1).

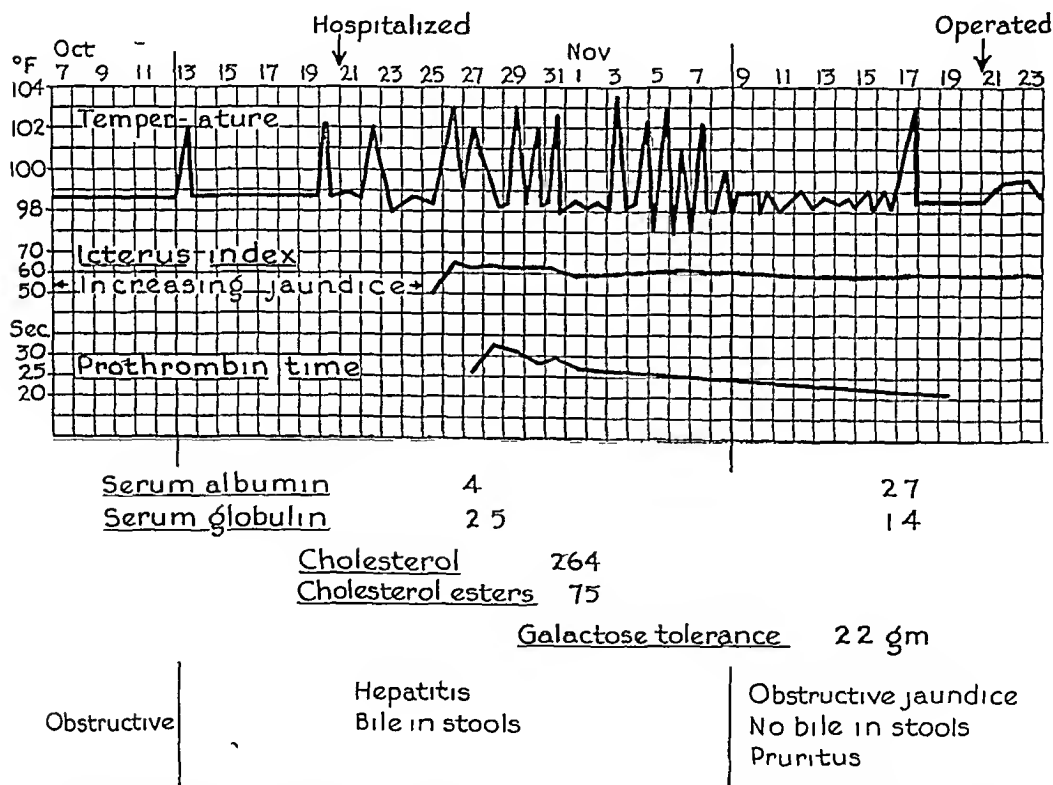


CHART 1—Showing temperature throughout various phases of illness. The level of icterus index and other laboratory studies are shown. Periods in which the jaundice was thought to be of intrahepatic and of extrahepatic origin are indicated.

His condition gradually improved, the fever subsided and he appeared less toxic. However, following the subsidence of fever, bile disappeared from the duodenal contents and did not return. The icterus index remained at 60, jaundice evidently persisting at this level because of obstruction to the extrahepatic ducts. Pruritus developed. Although low serum protein levels and a high return of galactose in the urine indicated considerable liver damage, the patient appeared improved clinically and as total obstruction to the bile ducts now existed, surgery seemed indicated.

At operation a fistula was found between the fundus of the gallbladder and the prepyloric portion of the anterior wall of the stomach. The lumen was almost obliterated. The gallbladder contained a number of calculi and one large stone was found in the distal end of the common duct evidently causing complete obstruction. The fistulous opening into the stomach was closed, the stone removed from the choledochus, and the gallbladder removed. Recovery was satisfactory but slow, the patient being dismissed on his nineteenth postoperative day. The jaundice did not entirely disappear for two months.

This patient presents an interesting sequence of events. The onset of jaundice evidently was due to the stone blocking the common duct and was purely obstructive in nature. Distention and inflammation of the gallbladder was followed by the establishment of a cholecystogastric fistula. Although this permitted free drainage of bile into the gastro-intestinal tract, regurgitation of intestinal contents into the bile ducts produced a severe cholangitis and hepatitis lasting three weeks. During this period the degree of jaundice remained constant but was due to hepatitis rather than to obstruction. The presence of bile in the stomach confirmed the patency of the fistula. I believe surgery at this time would have been extremely hazardous as no obstruction existed and the liver was acutely diseased.

After the chills and fever subsided, the fistula evidently closed and again his jaundice was on an obstructive basis. This was suggested by the subsidence of fever, the absence of bile in the stomach, the persistence of jaundice at the same level, and the development of pruritis. In spite of laboratory evidence of diminished hepatic function, the patient was clinically improved and surgery now seemed imperative to relieve the obstruction.

Fistulae between two portions of the extrahepatic biliary tract are rare. The one case in this series gave a four months' history with several attacks of severe right upper abdominal pain followed by chills, fever, and jaundice. At operation the cystic duct was found to be very small. A large fistulous opening formed a second communication between the ampulla of the gallbladder and the dilated and thickened choledochus. One large stone was removed from the distal end of the common duct and the gallbladder was completely excised.

The fistula existing between the common hepatic duct and the duodenum developed spontaneously, following damage to the choledochus during cholecystectomy. Biliary colics had occurred for several years prior to cholecystectomy but fever and jaundice were absent. Following operation jaundice developed and persisted almost constantly though varying greatly in intensity. One year later this patient came under our care, moderately jaundiced but with bile present in the duodenal contents. At operation a stricture of the common duct was found with a fistulous tract extending from the common hepatic duct to the duodenum. This was excised, the duodenal opening closed and a plastic repair of the common duct performed.

Fistulae originating at the liver or bile ducts and extending through the right diaphragm to communicate with a bronchus usually are due to gallstones, to amebic abscesses, or to hydatid cysts of the liver. There is often a preceding

history of biliary disease with evidence of an elevated right diaphragm and later pleural effusion. Bile in the sputum is the most diagnostic finding. The following case is of interest because the hepatobronchial fistula was secondary to streptococci abscesses of the liver and the patient recovered.

Case 2—A previously healthy, 26-year-old, white, male, developed general malaise, headache, and fever. After being treated for influenza for a week he did not improve and was hospitalized. His temperature ranged between 101° F and 104° F. The liver edge extended progressively lower and the right diaphragm steadily became elevated. Liver abscess was suspected but no improvement followed the administration of sulfanilamide or emetine. A right-sided pleural effusion was noted and gradually increased. This was soon followed by jaundice, shooting pains in the right upper quadrant, and tenderness over the liver. The appearance of bile in the sputum established the diagnosis of an hepatobronchial fistula. Three weeks after the onset of symptoms, an abscess high in the dome of the liver was drained through an anterior subcostal incision. This approach was used because it overlay the area of greatest liver tenderness. Nonhemolytic streptococcus was found in the abscess contents. Improvement followed this operation, bile disappeared from the sputum but drained freely from the wound and his fever subsided. One month after operation he again became febrile, bile returned to the sputum and abdominal pain recurred.

A second operation was performed, the twelfth right rib being resected and the subphrenic space entered posteriorly. In approximately the middle of the dome of the liver an abscess was found adherent to the diaphragm. The liver was separated from the diaphragm and a large cavity filled with necrotic tissue and pus was located in the dome of the liver. Again nonhemolytic streptococcus was found. Bile soon disappeared from the sputum. Drainage persisted both anteriorly and posteriorly for many weeks. The patient slowly improved and was discharged from the hospital three months after operation.

RESULTS

The mortality of surgery for internal biliary fistulae, generally, is considered to be much greater than for uncomplicated biliary tract disease and has been reported at 10 per cent or higher. In this series of 16 patients there were three hospital deaths, a mortality of nearly 19 per cent. This is very high when compared to our mortality of 12 per cent for uncomplicated cholecystectomies. Although two deaths, one patient with a cholecystoduodenal fistula, the other with a cholecystocolic fistula, were attributed to cardiac failure on postmortem examination, it is evident that the debility, liver damage, and prolonged sepsis associated with the internal biliary fistulae were largely responsible for failure of recovery. The third death occurred in the patient with a cholecystoduodenal fistula with associated duodenal obstruction. This patient's symptoms suggested gallbladder disease but as she firmly believed that her gallbladder previously had been removed, she refused surgery until duodenal obstruction was nearly complete and had resulted in marked emaciation and nutritional deficiency.

The morbidity of biliary surgery complicated by internal fistulae likewise is increased. The average length of hospital stay after operation was 23.5 days compared to 12.7 days for all other operations for benign biliary tract disease. The time required for the disappearance of jaundice, return of weight and strength, and ability to return to normal activities was several times that following surgery for uncomplicated biliary disease.

DISCUSSION

It has been stated that the development of a spontaneous internal biliary fistula is nature's cure of an obstruction to the bile ducts. That "the cure is worse than the disease" is well substantiated by the increased mortality of biliary tract surgery when fistulae exist. In this series of cases, the relief of symptoms which is claimed to follow the establishment of a new opening between the gallbladder and gastro-intestinal tract did not occur. Almost invariably the patients became progressively worse. Chills, fever, and leukocytosis indicated a severe inflammatory disease. Gradual weight loss and weakness indicated a disturbance of nutrition possibly on the basis of a damaged liver. Jaundice in the absence of obstruction was a very frequent finding and indicated cholangitis and hepatitis. As these symptoms are far more frequent and severe in the presence of fistulae than in other cholecystic disease, it is evident that the regurgitation of intestinal contents into the bile ducts is very damaging to them and to the liver. This is true whether the contamination be from the stomach, duodenum, or colon. However, colon contents seem to produce a more acute and virulent reaction. The chemical action of gastric or duodenal secretions may be a factor.

The distal end of the choledochus is provided with three important structures to prevent duodenal regurgitation. The sphincter of Oddi, although serving largely to regulate the flow of bile into the duodenum, may act as a barrier. The oblique course of the choledochus through the musculature of the duodenum utilizes the action of these muscles to compress the duct when tension in the duodenum is increased by peristaltic contraction. Most important, however, are the valve-like folds lining the ampulla of Vater which permit bile to flow out but very effectively prevent duodenal regurgitation. This can be demonstrated experimentally by greatly increasing intraduodenal pressure without forcing contents into the common duct. It is demonstrated clinically by the infrequency with which barium is noted to pass into the bile ducts during gastro-intestinal studies. When such regurgitation does occur, there is usually some pathological change in the distal common duct. Most often this consists of a fibrosis and destruction of the valves in the ampulla of Vater resulting from the passage of a large gallstone into the duodenum. Such protection against the entrance of intestinal contents into the bile ducts would hardly be warranted if these contents were harmless.

The experimental work of Beaver, and others, has shown that in animals, when free communication between the gastro-intestinal tract and bile ducts is established by cholecystogastro-intestinal anastomoses, progressive liver damage occurs. Liver damage has likewise been apparent in this series of patients with internal biliary fistulae, and has been demonstrated not only by liver function tests but also by the prolonged period of time elapsing after operation before jaundice entirely disappears.

The preoperative diagnosis of internal biliary fistula is being made more often with frequent and more thorough roentgenologic studies. Clinically the

- ⁴ Borman, C N, and Rigler, L G Spontaneous Internal Biliary Fistula and Gallstone Obstruction *Surgery*, 1, 349-378, 1937
- ¹ Courvoisier, L G Cavistisch statistische Beitrage zur Pathologie und Chirurgie der Gallenwege Leipzig, F C W Vogel, 1890
- ⁵ Dean, G O Internal Biliary Fistulas *Surgery*, 5, 857-864, 1939
- ⁶ Hunt and Herbst Quoted by Borman and Rigler³
- ⁷ Judd, E S, and Burden, V G Internal Biliary Fistula *ANNALS OF SURGERY*, 81, 305-312, 1925
- ⁸ Kehr Quoted by Borman and Rigler³

DISCUSSION—DR HUGH H TROUT (Roanoke Va) I would like to report a case of intestinal obstruction due to a gallstone, and the roentgenographic findings in the common duct Incidentally, we did not make this diagnosis before the gallstone was removed In taking a plain roentgenogram of an intestinal obstruction case we were very much surprised to find the common duct greatly dilated with air I do not know how many of you have seen intestinal obstructions due to large gallstones but I think you will find that is fairly common The gallstone passes through the common duct obstructs the duodenum and as the gas backs up the common duct is also dilated If you want to make a diagnosis of intestinal obstruction due to gallstones this may help you

DR JOHN M FINNEY, JR (Baltimore Md) Doctor Puestow said something about hesitating to speak about such minor surgery as internal biliary fistulae after the program which has preceded this paper From my experience this is not in the minor surgical class

I want to cite two instances which I think are rather interesting particularly the second one exhibiting complications which one may encounter with this type of case

The first case that I cite is one we saw a good many years ago, in which there were multiple biliary fistulae I do not think that this was entirely due to the surgical handling But when the gallbladder was finally isolated it was found that there was a fistula medially between the gallbladder and the stomach posteriorly between the gallbladder and the duodenum and inferiorly between the gallbladder and the transverse colon

The other case was one in which I was called to see suffering from profuse intestinal hemorrhage rather fresh and the patient was in bad condition The only history to which we did not attach any particular importance at the time was that of a prolonged illness of about three months duration 12 years previously with pain in the right upper quadrant and considerable wasting during that period of time We thought that the hemorrhage was possibly coming from a bleeding ulcer in a Meckel's diverticulum because while the blood was partially changed it came through fairly bright

The interesting finding, which we did not interpret before operation, was a large calcified shadow about the size of a good-sized orange in the region of the right lobe of the liver, which we considered to be a calcified cyst of some sort

With considerable difficulty and many transfusions the patient was prepared for operation at which time we found that the calcified body was a completely calcified gallbladder, which had become adherent to and perforated into probably 12 years previously the transverse colon and that a calcified piece had broken loose from the inside of this calcified gallbladder and had tried to pass through the fistula which was about 0.5 cm in diameter In so doing had severed a large vessel in the mesenteric margin of the transverse colon

This patient did not do very well and developed numerous fistulae He was readmitted to the hospital about five months later where he died eight months after the original operation of actinomycosis of the lung the chest wall the abdominal wall and liver presumably all of which was acquired at the time of the separation of the original fistula between the transverse colon and the gallbladder

DR JOHN A WOLFER (Chicago Ill) Doctor Puestow mentioned the matter of weight-loss also the prior history It reminded me of a patient I saw some years ago who so far as we could determine had no prior history of any acute intra-abdominal catastrophe He was seen at the hospital a diagnosis having been made of carcinoma of the hepatic flexure of the colon This was made upon a history of a weight-loss of 40 pounds relatively rapidly and a defect shown by barium enema

condition should be considered in patients with biliary colics accompanied by chills, fever, and jaundice, especially when these symptoms are frequent, persistent, and progressive. Frequent determinations of the presence and amount of bile in the duodenum is important both diagnostically and in determining the advisability and time of surgery. A persistent jaundice associated with a wide open biliary fistula which permits bile to flow from the bile ducts indicates that hepatitis exists and should make one cautious in instituting surgical therapy. As both the mortality and morbidity of surgery for internal fistulae are very high, good judgment and intensive preoperative care are essential. Likewise, the postoperative course is apt to be stormy and great care must be taken to protect the liver.

The calculi present in the choledochus of most of our patients found to have choledocholithiasis were formed in the gallbladder and passed through the cystic duct. Only a small percentage of these patients gave a history of persistent chills and fever and at operation acute cholangitis rarely was found. I believe that stones seldom form in the common duct in the absence of infection. However, when acute cholangitis exists, as is so frequently seen in internal biliary fistulae, stones may reform repeatedly in the bile ducts. This was demonstrated in the patient with a cholecystoduodenal fistula and severe cholangitis and hepatitis who had three common duct explorations for the removal of reformed stones.

SUMMARY

A series of 16 spontaneous internal biliary fistulae are presented. In evaluating the histories, pain, chills, fever, and jaundice generally were present. These patients did not obtain apparent relief of symptoms with the spontaneous establishment of a fistula, but became progressively worse.

At operation, stones were found obstructing the common duct in a majority of cases. Cystic duct obstructions were present in two.

Severe inflammation of the extrahepatic biliary system was present in most instances. This evidently resulted from contamination by intestinal contents. Liver damage of varying degrees likewise was associated.

Jaundice is a usual accompaniment of internal biliary fistulae and one must determine whether this is due largely to obstruction or to hepatitis. The degree of drainage of bile by the fistula as indicated by the amount of bile in the intestine is an important guide.

Stones may reform in the bile ducts in severe cholangitis.

Hepatic damage usually accompanies internal biliary fistulae and necessitates careful judgment as to the time of operation and intensive pre- and postoperative care.

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- ² Bernhard, Fr. Die spontanen inneren Gallenfisteln und ihre operative Behandlung. *Deutsche Ztschr f Chir*, 242, 493-506, 1934.

Upon operation there was found a granuloma-like mass involving the fundus of the gallbladder and hepatic flexure of the colon. The gallbladder was removed, the colon defect repaired, and strangely, following this operation he gained his weight just as rapidly as he had lost it. In the matter of two or three weeks he had gained back half his weight-loss and went on to uneventful recovery.

I was wondering whether one of two things might obtain: whether he lost weight by virtue of bile probably passing into the colon, so that it was not made available for use, or if he had an ascending infection which may have produced a varying degree of hepatitis which accounted for his weight loss. I do not know yet as to which of these factors might have obtained. To me it was unusual, and I was interested to hear Doctor Puestow say he had seen so many cases because when everything is said and done, I do not believe they are so common, and I am certainly glad they are not.

DR J DEWEY BISGARD (Omaha, Nebr.) About a year ago I explored a case upon a diagnosis of a choledochoduodenal fistula and found that I was in error. This is the film upon which the diagnosis (slide) was made, showing barium entering the common bile duct which persisted after the stomach was emptied of barium at the end of six hours. It also showed, in looking over the film subsequently, this filling and some dilatation in the duodenum. This patient had about an eight months' history of digestive disturbances which I will not go into, and had had a cholecystotomy, so had a background for this picture.

(Slide) At exploratory operation a primary lymphosarcoma of the duodenum was found, and this is the specimen which I resected by a one-stage Whipple operation. This shows the cause of the barium showing in the common bile duct. You see the wooden rod there passed through the distal end of the common bile duct and coming out in the center of this tumor, and either as a result of destruction of the ampulla or as a retraction from the tumor it has become incompetent and permitted the barium to enter the common bile duct.

I am showing this both as a possible error in interpretation of the roentgenograms, and also as an example of another indication for the Whipple operation.

(Slide) That is the other slide, showing the common duct in the upper part.

DR CHARLES B PUESTOW (closing) The cases that have been presented are very interesting, and I would like to make one comment. Three years ago next month while attending the meeting of the Swedish Surgical Society, a paper was read in which the recommendation was made to perform a cholecystogastrostomy or cholecystoduodenostomy for common duct stones, feeling that that was a safer procedure than to go down and explore the common duct. In view of what happens to the bile ducts and to the liver it seems to me that that procedure would be rather hazardous for the patient.

REFLEXES ORIGINATING IN THE COMMON DUCT GIVING RISE TO PAIN SIMULATING ANGINA PECTORIS*

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THE OCCURRENCE of gallstone disease with cardiac syndromes is now so well recognized that it would seem that further evidence on this relationship is hardly necessary. However, the frequency with which surgeons still see patients who have been classified as having serious cardiac disease, and who are simultaneously suffering from gallstone disease, but are denied surgical relief for the latter for fear of cardiac death, prompts us to make this report.

In 1909, Robert Babcock,¹ of Chicago, called attention to the frequent association of gallstone disease with heart disease. It is interesting to quote from his classic paper: "There is, however, another point of interest in this matter of the symptomatology of gallbladder disease, namely, the occurrence of disorders in the action of the heart, from arrhythmia and precordial oppression, without dyspnea, to demonstrable dilatation and incompetence, dating usually from some attack of biliary colic or acute cholecystitis, and thenceforth maintained by recurrences of the acute disturbance." He then concludes, after reporting 13 patients with this syndrome: "Experience has convinced me that the opening and draining of the gallbladder are attended with less danger when properly performed, even though myocardial incompetence be present, than is the doctrine of noninterference. Did time permit, cases could be cited which prove the peril to the patient from acute cholecystitis and fatal dilatation of the heart in cases with a history and symptoms of chronic cholecystitis, not to mention that from hepatic colic."

In 1935, Fitz-Hugh and Wolferth² pointed out that a "patient with gallstone disease may present such a convincing array of cardiac symptoms that the internist may wrongly condemn the sufferer to a 'life sentence' of cardiac servitude. In addition to this problem of mimicry there is a growing conviction among internists and surgeons alike that chronic disease of the gallbladder may either initiate or aggravate actual heart disease—especially so-called coronary heart disease."

Fitz-Hugh and Wolferth found that in numerous instances flat or inverted T-waves in the electrocardiogram prior to operation became erect and normal subsequent to adequate biliary tract surgery. They concluded that "in the present stage of our knowledge it would be idle to speculate as to the nature of myocardial disturbances responsible for the remarkable electrocardiographic

* Read before The American Surgical Association, Cleveland, Ohio, April 6-8, 1942

changes observed. It seems clear from the evidence, however, that not only may gallbladder disease injure the myocardium but that the process, at least to a certain extent, is reversible."

We have observed patients who have been decompensated for months and who had chronic auricular fibrillation restored to compensation and a regular cardiac rhythm with no change in the medical program following the simple removal of gallstones by cholecystostomy.

CASE REPORTS

Case 1—Hosp No 19622 P R, white, female, age 64, was admitted to the Hospital of the University of Pennsylvania, August 6, 1930, with a history of heart trouble over a period of eight years. She was short of breath, suffered from recurrent palpitation and right upper quadrant pain. For seven months she had been confined to bed. At varying periods she had had attacks of severe pain in the right upper abdomen associated with extreme nausea. She had taken digitalis for a number of years. She was markedly dyspneic and cyanotic. Examination of the heart showed this to be totally irregular. The heart was enlarged. The lungs were filled with moist rales at both bases. W B C 9,200. There was ankle edema. There could be no doubt but that she had cardiac decompensation. Whether the right upper quadrant pain was due to gallstone colic or to distention of the liver was not immediately clear. A roentgenogram of the abdomen disclosed a large gallstone.

She was operated on August 9, 1930, three days after admission. The gallbladder was drained and the stone removed. On September 5, 1930, she was discharged from the hospital in good condition, and with complete cardiac compensation.

This patient was extremely ill on admission to the hospital. Two of my colleagues, one a surgeon and one a cardiologist, considered her too sick for operation when first seen. Three days later, with her general state unchanged, she was operated upon. The operation did not upset her, in fact, she began to improve markedly immediately thereafter.

When seen three months later she was free of dyspnea and cyanosis. Cardiac rhythm was normal and she was attending to certain of her household duties.

We have seen patients with long-standing serious cardiac disease made hopeless invalids by the aggravation of their cardiac symptoms and the additional symptoms imposed by a gallstone-bearing gallbladder or the presence of stones in the common duct.

Case 2—Hosp No 42806 F B, white, female, age 53, was admitted to the Hospital of the University of Pennsylvania, August 30, 1939. She was told that she had a "leaky heart" after peritonitis at age 25. She claimed that she had no very distressing symptoms until one and a half years ago when she had an attack of palpitation associated with weakness which lasted several hours. At the same time she began to have attacks of "indigestion" associated with abdominal cramps and diarrhea, and pain in the upper abdomen radiating around to the right side of the back. Some of the attacks had been severe enough to require morphine, although minor attacks occurred every few days. Each of these attacks was followed by increased palpitation and weakness. There was no doubt in her mind that these symptoms were augmented, if they were not initiated, by the attacks of abdominal pain. Her condition became such

that her physician placed her on a program of restricted activity. She had never been decompensated.

She was found to have an old "rheumatic" mitral valve disease (stenosis and insufficiency) with some myocardial degeneration, extrasystolic arrhythmia, with episodes of auricular fibrillation. In addition, she was found to have gallstones.

A cholecystectomy was performed September 6, 1939. Following cholecystectomy she had three attacks of paroxysmal auricular fibrillation, after which these disappeared.

She still has her heart disease but 15 months after operation she remains greatly improved, is able to resume many of her previous activities, and is not fibrillating. Although she still tires easily the attacks of "palpitation" occur only at rare intervals.

There have been indications in some of these patients that the symptoms of existing coronary disease can be made worse by superimposed gallstone disease and what is more surprising is that gallstone disease may, at times, initiate a train of events with symptoms which in many particulars resemble true angina pectoris. We have seen a number of the patients who for variable periods of time have been treated as cases of true angina pectoris by men considered competent in the field of cardiology and who, following the removal of a gallstone-bearing gallbladder or stones from the common duct, or both, have had complete freedom from their supposed anginal attacks.

Recently, Layne and Bergh³ reported that sudden distention of the common duct in man caused reflex spasm at the lower end of the common bile duct, which they designated as spasm of the sphincter of Oddi. They found that the spasm thus produced resisted levels of pressure within the common duct as high as 400 to 600 Mm. of water, and in some instances persisted for as long as four minutes.

The apparatus used in these experiments consisted of a large glass flask, or reservoir, of about 75 cc. capacity, connected by rubber tubing to the T-tube in the common duct of the patient. A glass Murphy drip bulb is used to demonstrate the flow of fluid within the system. The pressure developed within the common bile duct is registered by a glass manometer.

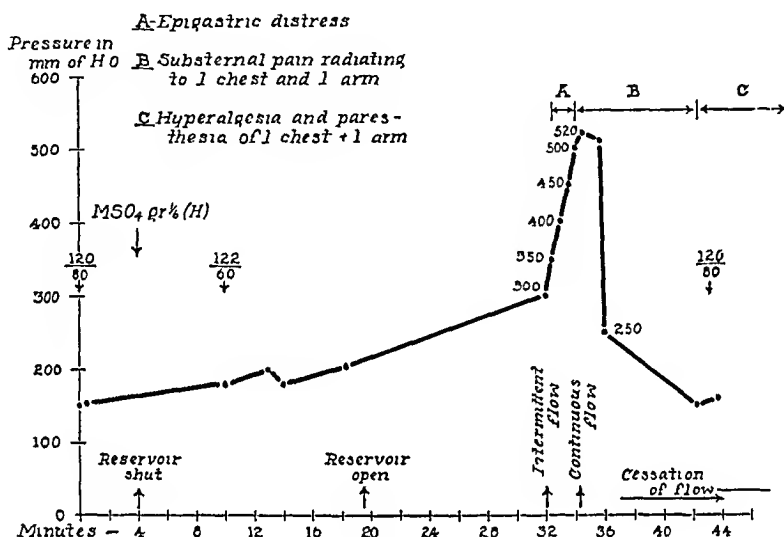
We wish to report the records of two patients in whom gallstone disease was associated with the symptoms of angina pectoris.

Case 3—Hosp. No. 43748 S. L., white, female, age 48, was admitted to the Hospital of the University of Pennsylvania for the second time, February 23, 1940, with a history of attacks of severe precordial pain, occurring mainly at night but occasionally after meals, and accompanied by palpitation and dyspnea. The precordial pain radiated through to the back and down the ulnar aspect of the left arm to the finger tips. Following these attacks the patient noticed residual soreness of the precordium and paresthesias of the left forearm and fingers of the left hand. The pain was sometimes relieved by large doses of nitroglycerin.

The attacks began about five years previously, six months after a cholecystectomy performed elsewhere. There was no history of jaundice, acholic stools, nausea or vomiting. Until the last attack of pain a few days before entering this hospital, she had had no attacks of abdominal pain, all previous pain having been precordial in location. In spite of all previous therapeutic efforts, the attacks of pain had become more severe and more frequent. A diagnosis of angina pectoris had been made in another institution,

and a left stellate ganglionectomy had been performed. No relief was afforded by this procedure, in fact, the patient became much worse. Frequent attacks of pain were now brought on by the mildest exertion, even by eating. Many of the attacks came on at night while the patient was sleeping. She had lost 44 pounds in weight and had become practically bed-fast.

In December, 1939, she was first admitted to the Hospital of the University of Pennsylvania. At this time ballistocardiographic studies were made by Dr. Isaac Starr, which showed an abnormally low cardiac output, thought to be indicative of myocardial damage. Alcohol injection of the second, third, fourth and fifth thoracic sympathetic ganglia on the left side was done at this time. The patient was discharged and readmitted February 23, 1940. During the interim she had become steadily worse. A few days before readmission she had experienced her first attack of definite abdominal



GRAPH 1

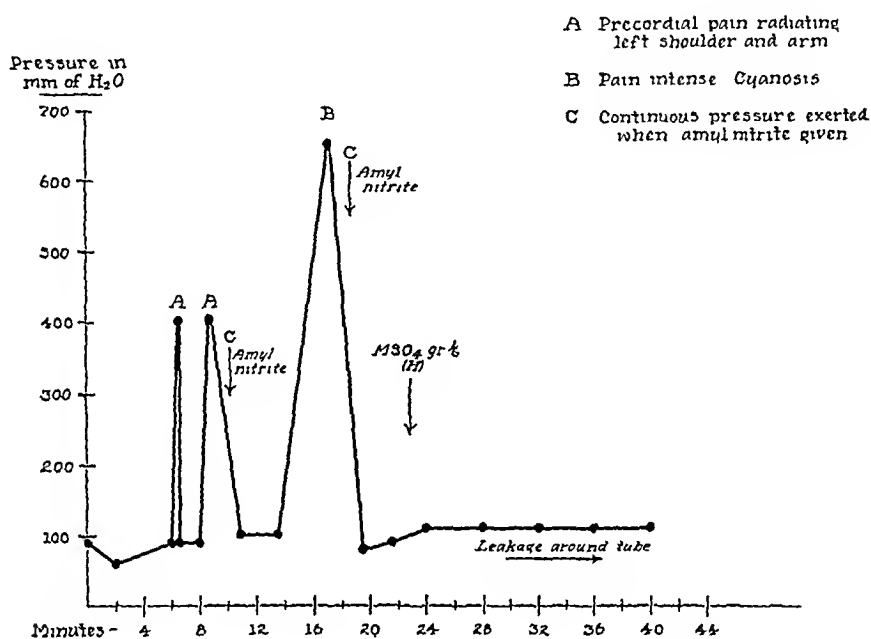
pain. This pain had been located high in the epigastrium and right upper quadrant. However, at this admission, it was thought that her electrocardiogram for the first time showed evidences of coronary artery disease and localized myocardial damage.

In view of the lack of results from previous therapy, and because of definite suggestion of a biliary tract origin for the patient's complaints, a celiotomy for exploration of the common bile duct was performed, March 22, 1940. A thick, kinked common duct was found, plastered with adhesions, and containing some "sand" but no stones. The duct was freed of adhesions, thoroughly irrigated and a T-tube left in place. Shortly after operation the patient declared that she was free of her former attacks of pain. She found that she could eat liberally without fear of discomfort. She was soon out of bed, and for the first time in five years, was able to walk about freely without recurrence of pain. Ballistocardiograms made at this time showed a normal cardiac output.

On the eighth postoperative day studies of common duct resistance were made (Graph 1). At the first severe distention of the common duct the patient complained bitterly of precordial pain, radiating down the ulnar aspect of the left arm, entirely similar to her previous attacks. She was very upset and had to be reassured that these pains were entirely a product of the procedures at hand, and not a recurrence of her old trouble. Distention of the common duct was repeated twice more on the same day, with exactly similar results. For several hours after the termination of these

studies, the patient complained of residual soreness in the precordium and of numbness and paresthesias of the left arm and hand. Four days later the experiments were repeated with similar results. At this time continuous electrocardiographic and ballistocardiographic tracings were made by Doctor Starr. Distention of the common duct was performed three times, and in each instance an anginoid attack was precipitated whenever the common duct pressure was raised to levels of 450 and 500 Mm of water. The severe precordial pain subsided promptly upon release of the high ductal pressure, leaving residual precordial soreness, and paresthesias of the left arm and fingers of the left hand. The electrocardiographic and ballistocardiographic tracings showed nothing significant except for a slightly diminished cardiac output during the periods of severe distention.

The patient was shortly afterward discharged, symptom-free, and has remained so to date, despite removal of the T-tube from the common duct.



GRAPH 2

Another patient in this series also gave a history of precordial anginoid pains suggesting coronary artery disease, prior to operation.

Case 4—Hosp No 10770 K T, white, female, age 45, was admitted to the Hospital of the University of Pennsylvania for the third time, December 9, 1940. She had previously had an appendectomy and a hemorrhoidectomy, with uneventful recoveries. Her blood pressure readings had never exceeded normal figures. Since 1933, seven years before admission, she had experienced recurrent attacks of pain in the left side of the chest under the left breast with radiation to the left shoulder, produced by physical exertion or mental strain. She also had shortness of breath on exertion and swelling of the ankles. The attacks of this pain soon recurred so frequently that she could not perform her household duties and she became a semi-invalid. She was seen in the Robinette Foundation and a diagnosis of angina pectoris was made, on the basis of arteriosclerotic heart disease. In September, 1940, she first experienced an attack of intense pain in the right upper abdominal quadrant. The attack was accompanied by nausea and slight jaundice. Subsequently, she was studied in the gastro-intestinal department and a diagnosis of cholelithiasis was made. She had several more similar episodes of abdominal pain.

On December 13, 1940, cholecystectomy and choledochostomy were performed. Gallstones were found in the gallbladder, but exploration of the common duct revealed none. Following operation the patient was able to sleep on her left side for the first time in several years. She had no further attacks of pain, and when ambulatory was entirely comfortable and experienced absolutely no pain.

A pressure study of the common duct similar to the one described above, was carried out on this patient (Graph 2). When the pressure was raised to a level of 400 Mm. of water pressure the preoperative anginal type of pain occurred. The pain ceased immediately upon reduction of the pressure. When the pressure was maintained at a high level, it was reduced gradually upon administration of amyl nitrite. It is interesting to note that the original anginal attacks were partially relieved by this drug. The ballistocardiographic tracing showed no abnormality before operation, after operation or simultaneously with the rise in pressure. Negative results were obtained with the electrocardiograph.

A cholangiogram was made through the T-tube and the films showed a narrowing of the lower end of the common duct. It is quite possible that an associated pancreatitis caused the slight jaundice. Four weeks after discharge the patient returned for another cholangiogram, and the duct was found to have become slightly larger. Follow-up examination, nine months later, revealed that this patient was completely relieved of all pain.

Bellet and Meade,⁴ in our laboratory, have attempted to produce significant changes in the electrocardiogram of the dog by distention of the gallbladder or common duct. They obtained no major changes in the electrocardiogram unless prior to distention of the biliary tract some minor abnormality had been produced in the coronary blood flow. When even a small coronary vessel had previously been ligated, abnormalities in rhythm and conduction were obtained.

The subject of viscerocardiac reflexes has been well summed up from the physiologic aspect by Scott and Ivy.⁵ They conclude that (1) Changes in cardiac rate, rhythm, and output can be caused by distention of the common bile duct in dogs, (2) such changes are inconstant, variable, and unreliable, (3) success or failure in the production of such changes by common duct distention depends on the presence or absence of functional or organic cardiovascular abnormality at the time the distention is carried out.

Baker, Wilson and Coller,⁶ and others, have reported cases of abdominal disease simulating coronary disease. In three of their four cases, the electrocardiogram was normal. In the fourth, it showed definite evidence of coronary artery disease. All were cases of cholelithiasis and cholecystitis, and all were relieved of their symptoms by operation.

Recently Gilbert, and his associates,^{7, 8} have published important contributions in this field. They have shown that there is a decrease in coronary blood flow upon distention of the gallbladder or distention or irritation of its ducts. Gilbert has called attention to the fact that both clinical and experimental evidence indicates that stimuli originating in the gallbladder may cause a decrease in the coronary blood flow which results in a disproportion between blood supply and blood needs similar to that which occurs when intrinsic anatomic changes are present in the vessel walls. In the one instance pain

is the result of spasm induced by extrinsic autonomic stimuli, in the other the disproportion becomes evident when additional demands are made upon the restricted supply of blood in the coronary vessels. The degree to which intrinsic and extrinsic factors are involved in bringing about a restriction in coronary blood flow without doubt varies greatly in different patients and accounts for the variability of the preoperative and postoperative symptoms. While the intrinsic factors may be irreversible, the extrinsic factors are reversible provided their cause can be eradicated.

Distention of the common bile duct in the presence of muscular irritability at the lower end of the duct will cause reflex spasm in this region and physiologic blockage of the duct. It is important to the investigator to realize that after the administration of morphine sulphate, gradual distention of the duct such as obtains during experimental determinations of sphincter resistance or perfusion pressure also causes reflex spasm nearly as marked as that produced by rapid distention under the same conditions. For this reason, values for perfusion pressure obtained after the administration of morphine sulphate necessarily have a wide range, from the levels of pressure at which definite flow is first noted, to the high levels of pressure needed completely to overcome the vicious cycle of reflex distention-spasm. After morphine sulphate, then, even small increments of common duct pressure will promptly produce reflex spasm, which in turn raises the perfusion pressure level necessary to overcome resistance to flow in the common duct. To overcome resistance at this new level, additional increments of pressure are necessary, but these, by their distending effects, produce still more spasm and increase the perfusion pressure value still more. Thus a staircase phenomenon of increasing perfusion pressure values is produced before peripheral ductal resistance is completely overcome at a very high level of pressure.

The observations of Best and Hicken,⁹ Doubilet and Colp,¹⁰ and McGowan, and his associates,¹¹ demonstrate that degrees of irritability in the duodenocholedochal region sufficient to cause biliary tract pain are often encountered in certain types of patients. Layne and Bergh have reported no cases in which this irritability was of sufficient magnitude that mere sudden distention of the common duct in these patients created severe reflex spasm, and a high degree of mechanical obstruction of the common duct. In the present studies, comparable degrees of spasm have been produced by sudden distention only after the administration of morphine sulphate.

SUMMARY

We believe, however, that these are the first reported patients in which anginal attacks have been consistently reproduced experimentally in man, by distention of the common duct.

It can now be safely assumed that gallstone disease or disease of the common duct may aggravate the symptoms of preexisting heart disease. Reflexes arising in the extrahepatic bile passages may at times bring about

a restriction in coronary blood flow which produces the symptoms of angina pectoris. When the extrinsic factors giving rise to these reflexes are removed, the anginal symptoms disappear. Similarly such reflexes may further decrease the coronary blood flow brought about by intrinsic changes in the coronary vessels. While adequate surgery does not completely relieve the patient of his cardiac symptoms, some measure of relief is nearly invariably obtained.

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DISCUSSION—DR CHARLES G MIXTER (Boston Mass.) Doctor Ravdin has brought clearly to our attention a problem that is always difficult—has the patient biliary tract disease, coronary disease, or has he both? Furthermore, he has emphasized the part that biliary tract disease may play in the aggravation of the concomitant heart disease. Finally, he has been able to reproduce in patients in whom the common duct pathology has been removed the anginal symptoms by distention of the common duct.

Left-sided pain in biliary tract disease is usually explained by pancreatitis or an extension of the pericholecystic disease to the left side. Rarely, pain may occur on the left side without extension of the inflammatory process. On embryologic grounds, the common duct must be assumed to have a bilateral innervation. This would explain the occurrence of left-sided pain.

Recently, Doctors Fine and Starr, of our clinic, have reported two cases of crossed pain in biliary tract disease. The first patient was a female, age 45, with an eight-year history of severe stabbing pain, starting in the epigastrium and radiating around the left costal margin and to the left scapula, occasionally to the left shoulder, arm and finger tips. The attacks were not related to food, exercise or rest. A cholecystectomy had been performed six years previously. The gallbladder had contained stones. The common duct was normal to palpation and was not opened. Recurrence of attacks of pain in the chest led to a diagnosis of angina. There were no jaundice and no gastro-intestinal symptoms. The electrocardiogram and glucose tolerance curve were normal. Duodenal drainage yielded crystals. At operation a single pea-size stone was removed from the common duct. She has been symptom-free for two years.

Case 2 was a female, age 71. Her first attack occurred one week before entering the hospital, and she had had nightly seizures of girdle pain, of equal intensity on both sides. The electrocardiogram showed a probable intraventricular block. The icteric index was 15. Cholecystogram showed cholelithiasis. At operation a small gallbladder, containing stones, was excised, and stones were removed from the common duct. During convalescence clamping of the common duct drainage tube initiated pain. At other times she was symptom-free. A cholangiogram revealed a small residual stone. To establish a relationship between the common duct stone and the preoperative left-sided pain, saline solution was injected both slowly and rapidly, with a reproduction of the pain along the left costal margin and in the left scapula. There was no pain reference to the epigastrium or right side. It was

felt this procedure forced the calculus into the duodenum, as a subsequent cholangiogram failed to show a stone. Removal of the tube was followed by rapid closure of the sinus and there has been no recurrence of the attacks of pain.

There is a small, but distressing, group of cases in whom symptoms persist after cholecystectomy with or without a demonstrable lesion of the common or hepatic ducts. In these, severe attacks of pain persist without associated fever, jaundice or elevation of white blood cells. Dyskinesia of the biliary tract has been discussed in the literature for some years. Dilator drugs usually give transient relief and gradually, over a period of months, cessation of symptoms occurs. Occasionally, one sees a case characterized by more severe pain suggestive of definite biliary colic in whom benzedrine or atropine give no relief, and in whom the symptoms persist.

An example of this type of case occurred in an intelligent woman of about 40. Following cholecystectomy for stones, colicky pain without jaundice recurred. A number of months later her common duct was explored but no pathology was demonstrated. Her convalescence was uneventful except that every time the common duct tube was clamped an attack of colic was brought on. After prolonged drainage the common duct tube was removed, the sinus healed readily but attacks persisted. Finally, a dorsal sympathectomy with resection of the great splanchnic nerve and removal of the lower three dorsal ganglia was undertaken by Doctor Smithwick. The patient has been free of symptoms for over two years. We have had two other similar cases in whom dorsal sympathectomy has afforded relief, but the time that has elapsed since operation has been too short to venture the assertion that they have been cured.

DR GEORGE J HEUER (New York) Doctor Ravdin's paper has brought up a great many interesting questions in this matter of association between gallstone disease and heart disease.

One of the interesting things that we found in a study of a fairly large series of cases of gallstone disease was that a rather high percentage of the patients with gallstone disease who arrived at age 50 or over, had cardiorenal disease and hypertension. In comparing this group of cases with such information as we could get from life insurance statistics it was evident that patients in our series who were over 50, and had gallstones, had in a much higher percentage of complications, if you want to call it that, such as heart disease and hypertension than we could find occurring in the normal population of the country in the same age-group. I hope that Doctor Ravdin will indicate whether that has been his experience.

The question again arises as to whether gallstones in some way provoked these conditions in a higher percentage of cases or whether patients with these conditions were more prone to gallstones. This is very difficult to get at, of course and I doubt whether one could arrive at a definite answer, but, certain it is, I think from our series of cases—and they number some 1200—we have studied—that there is a higher incidence of these cardiorenal conditions with hypertension in the age-groups over 50, than occur in the population ordinarily.

DR FRANK K BOLAND (Atlanta, Ga) We have had some reference this morning to historical medicine and it is with the object of reminding you of another historical fact that I rise. This historical fact also illustrates to us the diagnostic clinical acumen of some of the forefathers in medicine, who worked without electrocardiograms and without roentgenograms.

You will recall that John Hunter died in a hospital committee meeting from an attack of angina. Hunter's physician was none other than Edward Jenner. Hunter was known to have these heart attacks, but Jenner insisted that he also had gallstones. The point I wish to give you is that the autopsy revealed that Jenner was right and that John Hunter had gallstones and also had coronary sclerosis.

DR JOHN A WOLFER (Chicago, Ill) Along the line of Doctor Ravdin's presentation I want to put two side-lights on record. One was in a woman of about 60 years of age, upon whom I had performed a radical mastectomy. A short time after the

operation she developed typical precordial pain, radiating down the left arm associated with some dyspnea and slight cyanosis. The electrocardiogram was typical of coronary disease and as the symptoms progressed further study revealed that she had a small diaphragmatic hernia and when the diaphragmatic hernia was filled with food she had the typical electrocardiographic findings of coronary disease and when the gastric pouch was empty her electrocardiogram was perfectly normal.

The other is a reversal of the syndrome exemplified by this case. A man from South Carolina was diagnosed as having a fulminating acute cholecystitis with fever of 102° F and leukocytosis of 22,000. He was seen by a surgeon in that community who refused to operate upon him because of the severity of the symptoms. He recovered, went to Florida and I saw him the next spring.

His history was perfectly typical of chronic cholecystitis having right upper abdominal pain, distress after eating and nothing which would suggest cardiac disease. A study of the gallbladder revealed it functioned normally. Further study revealed nothing organic in his gastro-intestinal tract. The next morning he was found dead in bed. At autopsy there was found an enormous scar in the heart which I can only describe to you as looking like the bottom of a white china saucer. Almost the entire myocardium had been replaced by a scar tissue. Yet the man gave a typical gallbladder story so much so that Doctor Case when he examined his gallbladder he made a little note after his interpretation saying "I hope that my negative cholecystographies will not deter Doctor Wolfer from taking this man's gallbladder out." Yet he had no gallbladder disease, and his history would indicate he did have the effort syndrome. In other words he became distressed when walking and developed indigestion and pain with walking. But beyond that there was nothing.

By the way the electrocardiogram was reported "Nothing significant found."

DR HARRY B. ZIMMERMANN (St. Paul, Minn.) We have sufficient diagnostic machinery for limited diagnosis of gallbladder disease but quite often the question comes up as to whether one wants to use surgical therapeutics in the presence of cardiac disease. I am fairly convinced that there is something to the modern idea that atheromatous disease has a great deal to do with metabolic reverses. Quite often disease of the extrahepatic biliary tract besides gallbladder can aggravate such disturbances in the metabolism and I would not hesitate in persons with fairly definite atheromatous disease and cardiac disease to use surgical therapeutics.

DR I. S. RAVDIN (closing) I think the observations that Doctor Mixer and Doctor Smithwick have made in the patients with dyskinesia are very important observations because everyone interested in the surgery of the extrahepatic biliary passages must have seen a group of patients who continued to have colic even though there remain no stones in the common duct.

I am sure that Doctor Heuer's observations are correct ones. There is a higher incidence of cardiac disease in patients with biliary tract disease, patients with stones and a greater incidence of hypertension in the patients past 40 years of age—I believe Doctor Heuer said 50—than there is in the population at large.

Doctor Wolfer's observation merely accentuates the fact that we must be exceedingly careful in attempting to arrive at an accurate diagnosis. We have however seen two additional patients whom had we followed our inclination we might not have operated upon and the patients would certainly have died. Two patients with acute obstruction of the common duct who immediately went into shock so that it was impossible to record either their systolic and diastolic blood pressure. They were operated upon under continuous spinal anesthesia at a time when blood pressure could not be recorded. Immediately after drainage of the common duct the blood pressure returned so that it could be recorded.

This merely goes to show that both of these individuals were diagnosed, initially as having enormous cardiac infarctions. Both of these individuals showed evidence of preexisting cardiac infarction. Both of them survived operation well, and have done well since operation. It merely further emphasizes the fact that one can, by having reflexes which arise in the extrahepatic biliary passages, so accentuate intrinsic existing disease of the coronary vessels as to set up a train of events which produces nearly complete

cardiac incompetency and which can be relieved providing the mechanism which initiates these reflexes is relieved

I am perfectly sure that many of these individuals that are not now being operated upon should be, and our experience has shown that the risk of operating upon these individuals, properly prepared before operation and properly taken care of during operation, is not great. At the present time everyone is being operated upon with continuous spinal anesthesia, which I believe, in this group of patients, provides the greatest safe guard



WAR SURGERY

The outstanding feature of the surgery of the present war as compared with that of the last, was the almost complete disappearance of the ward dressing trolley and the war gas apparatus. The appalling pain caused by the daily, or twice daily, dressings had gone and in its place was the modern technic of excision and fixation. Fixation was practically always by plaster of Paris, although in the wounds of the thigh in fat women complete fixation by this means was an extreme difficulty. An addition to the technic was the use of sulfanilamide by packs or in powdered form or by insufflation on the surface of the wound, although the use of sulfanilamide had helped to prevent sepsis in some cases which had not come for operation for four to eight hours after the infliction of the wound, nothing could replace the perfect excision of the wound, which was the essential point in the treatment. Nothing was so criminal as to suggest that the excision could be done badly so long as sulfanilamide was used. The main problems met with now were shock for which fortunately the treatment was almost standardized, the prevention of sepsis, which depended largely on the excision of infected and dead tissues and the wide opening-up of tissues which had become infected and fractures of the pelvis, which had occurred more frequently than normal owing to the falling in of bombed houses. In many of these cases of fractured pelvis there was a rupture of the urethra, and it would be well if agreement could be reached on the ideal treatment of this complication.

—T. P. McMurray at a meeting of the Liverpool Medical Institution as reported in the British Medical Journal

THE SURGERY OF CARCINOMA OF THE PANCREAS AND AMPULLARY REGION*

REPORT OF SIX ADDITIONAL CASES

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AND

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THE SURGICAL TREATMENT OF CANCER of the pancreas and ampullary region has received recently increased attention. The successful removal of large portions of the pancreas, together with the ducts,^{5,9} has been reported by various authors. This experience has modified some of the established concepts of the physiology of the pancreas, and particularly concepts regarding the indispensability of the external secretions of this organ.

The successful removal of cancers in this hitherto inaccessible region has encouraged internists to review again the early signs and symptoms of this disease,¹ in the hope of finding more patients with the disease still in an operable stage. Since no one individual has acquired a large experience in the management of these patients and since the surgical technic is still in the developmental stage, the authors wish to present six additional cases for discussion.

CASE REPORTS

Case 1—History No 7023 W P, male, age 48. Admitted June 18, 1932. Six months—attacks of subscapular pain, five months—glycosuria, three months—abdominal pain on reclining, relieved by standing, two months—constipation, anorexia, weakness, weight loss. Small left abdominal tumor. Diagnostic exploration, cancer, body of pancreas. Splenectomy and subtotal resection of pancreas. Recovery. Died five months postoperative.

Chief Complaint—(1) Pain in the back and stomach (2) Weakness

*Present Illness—*Onset January, 1932, with dull, nonradiating, left subscapular pain in attacks lasting one to two days, increasing in frequency to admission. In March, 1932, he experienced a sensation of heaviness in the upper abdomen, described as "feeling as though the stomach were all cramped-up." This pain was relieved by standing up, leaning forward or flexing the thighs on the abdomen. This sensation, which he felt during the whole day, had recently been waking him from sleep at night. There had been increasing constipation and weakness with a weight loss of 15 pounds in two months. In February, 1932, during an insurance examination, a small amount of sugar was found in the urine and this had been verified on subsequent tests.

Past History was negative except for bleeding hemorrhoids.

*Physical Examination—*Showed a well-developed but emaciated man, with pale and sallow complexion. "He had the general appearance of a person suffering from malignancy." General oral sepsis and carious teeth. Abdomen showed slight tenderness in the epigastrium and just to the left of the midline was an indefinite small palpable tumor mass. Remainder of examination was irrelevant.

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

Laboratory Data—Fasting blood sugar On admission—79 mg, two hours after ingestion of 50 Gm of glucose—128 mg Repeat fasting—130 mg Urine Normal, no sugar Blood R B C 35 Hemoglobin 95 per cent W B C normal Repeated stool examinations showed presence of bile and no blood or other abnormalities Gastric analysis Fasting—HCl 1 cc, after histamine—HCl 10 cc Roentgenograms of the gastrointestinal tract and lumbodorsal spine negative

Operation—S C H July 6, 1932

Preoperative Diagnosis—Retroperitoneal tumor

Postoperative Diagnosis—Carcinoma of the body of the pancreas

Procedure—Splenectomy and subtotal excision of the pancreas

A left upper rectus incision was made On exploring, it was found that a dense mass, measuring 4-5 cm in diameter, lay directly over the aorta in the midline at the level of the pancreas By dividing the gastrocolic omentum so as to give exposure to the pancreatic region, it was found that this mass lay in the body of the pancreas, and that excision of it meant an excision of the pancreas An attempt was made to work around the mass from above and below, but it was found quite impossible to establish the exact line of cleavage Consequently, the spleen was freed from the parietal peritoneum inward toward the midline, the tail of the pancreas elevated and then dissection proceeded with, posteriorly, until the pancreas was freed up as far as the underlying superior mesenteric artery Dissection was then started at the head of the pancreas and it was found possible to get between the tumor mass and its attachment to the duodenum The pancreas was divided between crushing clamps, leaving a ribbon of pancreas 1 cm wide on the duodenum The dissection then proceeded to the left and the splenic vein was identified as it entered the portal vein and largely surrounded by tumor tissue The portal vein was isolated from the tumor mass and a clamp placed across the splenic vein at its junction with the portal vein and divided Dissection was then carried medialwards, the mass dissected off the hepatic artery and the superior mesenteric artery, the splenic artery then being ligated and divided and the mass removed The large intestine covered the raw area The wound was closed without drainage

Postoperative Course—The patient had a rather stormy course for the first 12 hours postoperatively, but thereafter made a rapid and steady gain Repeated uranalyses before and after operation, including routine diabetic fractional specimens four times daily, revealed only a very infrequent small trace of sugar Repeated stool examinations postoperatively revealed no evidence of failure to digest fats The patient was discharged from the hospital 17 days postoperative, with instructions to follow a diet of 70 Gm protein, 100 Gm fat and 200 Gm carbohydrate He tested his own urine Follow-up on this diet revealed that he gained weight, had an excellent appetite and no difficulties with digestion or sugar in the urine He died five months postoperative, probably of metastases, although no postmortem examination was obtained

Pathology Note—The pancreatic tissue was exceedingly firm and on section its normal architecture was entirely lacking, being replaced by coarsely granular, yellow-gray tissue There were no areas of hemorrhage or calcification There was one large lymph node found to contain tumor tissue Microscopic examination confirmed the gross impression of an extensive destruction and fibrosis of pancreatic tissue Even large blood vessels were occluded by fibrosis The tumor was an adenocarcinoma invading lymph nodes and along nerve sheaths There were numerous mitotic figures and a tendency to acinar formation

Comment This patient was the first of our series, and while a tentative diagnosis of carcinoma of the pancreas was made, it was by no means certain He had a six-months history of pain, now recognized as characteristic of carcinoma of the pancreas, namely, pain worse on reclining and relieved by leaning forward or relaxing the abdomen In spite of removal of all but a small fraction of the pancreas he showed no sugar and gained weight on a

mild limitation of diet. There were no evident disturbances of fat metabolism. He had lymphatic metastases at operation, and while the cause of death is unknown, it was likely due to extension of the tumor. An earlier diagnosis or exploration might have yielded a successful result.

Case 2—*History No. A94807 L P, male, age 60. Admitted July 17, 1939. Two months—itching, jaundice, weight loss 26 pounds. Transduodenal resection cancer of ampulla, with reimplantation of common and pancreatic ducts. No evidence of recurrence two years eight months. Living and well.*

Chief Complaint—Itching

Present Illness—Began a little more than two months before admission with itching, shortly followed by jaundice, clay-colored stools and dark urine. Although his appetite and digestion were said to have remained excellent, he had lost 26 pounds weight. He had no pain.

Physical Examination—Positive findings were a deeply jaundiced skin, with many small red annular lesions, eyes sunken, sclerae icteric, retinal arteriosclerosis, mouth septic with advanced caries, abdomen slightly distended and tympanitic, slight tenderness in right upper quadrant, where a smooth, firm liver edge was felt 2 cm below costal margin. The spleen could be felt on deep inspiration. He also had bilateral inguinal herniae, and a diffusely enlarged prostate.

Laboratory Data—Urine Normal except for bile 4+. Blood Normal. Icteric index 60 units. Liver function (bromsulfalein) five minutes—85 per cent dye retention, 30 minutes—45 per cent dye retention. Stools Normal except for absence of bile. Roentgenologic gastro-intestinal series and intravenous cholecystogram negative. *Impression*—Carcinoma of head of pancreas or ampulla.

Operation—A W O August 2, 1939. Transduodenal Excision of Carcinoma of Ampulla of Vater. The liver was found to be enlarged, the surface was rough and granular in appearance with some cirrhosis. The gallbladder was markedly dilated and the common duct 2.5 cm in diameter. Palpation revealed no evidence of stone. The only abnormal finding, and that indefinite, was a small soft mass in the region of the ampulla. The second portion of the duodenum was mobilized and a longitudinal incision made in it opposite the ampulla. A flat, cauliflower growth was found arising from the ampulla. It was 1 cm in thickness and 3 cm in width, with a papillary structure. A portion of this was excised for biopsy which was reported benign. A probe could be readily passed into the pancreatic duct but the common duct was completely obstructed. The tumor was resected by a circular incision 3 cm in diameter, the base of the tumor being 1 cm in diameter. The incision was carried through all layers of the duodenum and thence across the ducts at a depth of 2 cm. As the common duct was cut there was a free flow of bile. The cut ends of the common and pancreatic ducts were then mobilized and sutured together with fine interrupted silk. The edges of the duodenal mucosa were then sutured to the common and pancreatic ducts, forming a slight pit. It was necessary to do some slight mobilization of the duodenal mucosa in order to accomplish this. The opening in the duodenum was then closed in the usual manner. No drains were used.

Postoperative Course—This was smooth and he made an uneventful convalescence. A postoperative check-up film was taken showing the defect in the duodenum. Repeated roentgenograms since have shown no evidence of recurrence, and the patient continues in good health with no complaints.

Pathology Note—The biopsy had been taken from the surface of the cauliflower tumor. The pedicle was firm and extended into the common duct, completely occluding it and invading the wall of the pancreatic duct. Microscopic examination revealed the base of the tumor to be adenocarcinoma, Grade II, apparently arising in the base of a papilloma. There appeared to be an adequate margin excised.

Comment—This patient had a papillary cauliflower tumor apparently arising within the common duct, since this was completely occluded. The pancreatic duct was involved but still patent. The soft, flattened, sessile character of this tumor permitted it to blend with the duodenal wall in such a manner that it was not visualized roentgenographically. While the tumor was completely removed, as shown by histologic examination, and there has been no evidence of recurrence in two years and eight months, nevertheless, the question may be raised as to whether this type of local excision was adequate treatment of this condition. This was the only patient in this series with the classical syndrome of painless jaundice.

Case 3—*History* No B6323 J B, male, age 70. Admitted May 16, 1941. One year—*anorexia, nausea, vomiting and weight loss*. Three weeks—*pain and jaundice, hepatomegaly, epigastric mass, roentgenographic deformity of duodenum, two-stage operation*. Cholecystojejunostomy entero-enterostomy, resection of duodenum and head of pancreas, gastrojejunostomy. *Recovery*. Sudden death three months postoperative.

Chief Complaint—Abdominal pain and nausea.

Present Illness—He first came to the Medical Clinic in July, 1940, at which time he was examined to determine the cause of his complaint of anorexia, nausea, vomiting and weight loss of 20 pounds. Impression was that of generalized arteriosclerosis and hypertension, aneurysm of abdominal aorta, and probable duodenal ulcer. Laboratory data was essentially negative, including gastric analysis. At that time he had a question of clay-colored stools for a short period. Roentgenologic examination was advised but the patient did not return until ten months later, May 16, 1941. During this interval he continued at his work but suffered off and on with dull intermittent abdominal pain.

Three weeks before admission he noticed jaundice for the first time, which became progressively more intense, followed by itching. At the same time the dull intermittent epigastric pain became more severe. The abdominal throbbing which had been present since July, 1940, remained the same. He became constipated and his stools were white, although his diet had been restricted to skimmed milk, eggs and fat-free foods. With the onset of the present illness he developed shortness of breath and dyspnea. He had lost 15 pounds in the past month.

Physical Examination—Showed a chronically ill, emaciated, jaundiced elderly man. Positive findings were oral sepsis and carious teeth, a slightly distended abdomen with audible and visible peristalsis, dilated epigastric veins, liver extended to anterior superior iliac spine and was nontender, with a sharp, firm, irregular edge. In the mid-epigastrium there was a hard mass adjacent to the aorta. There was pitting edema of the feet with generalized arteriosclerosis.

Laboratory Data—Blood RBC 3.06, WBC and smear normal. Blood sugar (fasting) 83 mg per cent. NPN 33 mg per cent. Icteric index 100 units. Van den Bergh Direct reaction 20 seconds, indirect reaction, 27 mg/100 cc. Prothrombin time normal. Serum proteins 5.63 mg per cent, serum albumin 3.03 mg per cent, serum globulin 2.60 mg per cent. Stools Clay-colored, bile and blood negative. Blood studies (fats) Serum titrated fatty acids 100, serum lipoid phosphorus 80 mg per cent, serum total cholesterol 159 mg per cent, serum unesterized cholesterol 53 mg per cent. Liver function (bromsulphalein) 20 minutes—50 per cent dye retention. Gastric analysis Free HCl—33 units, after histamine, free HCl—74 units.

Roentgenologic Examination—(1) Narrowed and deformed distal first and proximal second duodenum (probably primary carcinoma of biliary tract, with secondary involvement of duodenum), (2) diverticulosis of colon and (3) atypical small intestinal pattern (deficiency state).

Operation—A W O May 27, 1941. Cholecystojejunostomy, Entero-enterostomy. An

upper right rectus incision was made. The liver extended to the crest of the ilium and was a deep purplish color mottled with yellow, with a coarse granular surface. The gallbladder and common duct were markedly distended. A movable tumor was found in the head of the pancreas about the size of a tennis ball. There was no evidence of metastasis. The jejunum was divided about three feet below the ligament of Treitz and an end-to-side anastomosis was performed, leaving a proximal blind end about 18 inches in length which was anastomosed to the fundus of the gallbladder. The wound was closed without drainage.

The patient made an uneventful recovery, and in four days the icteric index had dropped to 15, and bile was present in the stools. The patient's appetite improved, he put on weight, was ambulatory, and his deficient state seemed reasonably well corrected. Bromsulphalein liver function test showed 4 per cent dye retention in 30 minutes.

Second Operation—A W O July 16, 1941. Resection of Duodenum, Head and Part of Body of Pancreas, with Posterior Gastrojejunostomy. An upper right rectus paramedian incision was made. The adhesions from the previous operation were readily divided and the duodenum was exposed. The tumor was found to be about one-half the size it had been on the previous operation and it was more freely movable. The lateral border of the duodenum was readily mobilized and turned up off the vena cava, exposing the under surface of the pancreas. The inferior portion of the duodenum was readily dissected free, passing underneath the colic vessels in the mesentery and entering the free peritoneal cavity at the ligament of Treitz. No bleeding was encountered during this part of the procedure. The right gastric and gastroduodenal arteries were ligated and the pylorus was mobilized, clamped and divided. The jejunum was picked up at the ligament of Treitz. The anastomosis to the gallbladder had been far enough down the bowel so that there was ample jejunum. A posterior gastrojejunostomy was performed in the usual manner. The common duct was then isolated, divided and triply ligated with silk. The ligatures were spaced 0.5 cm apart, the proximal being not too tight and the distal transfixed. The dissection was then carried along the portal vein from below upward, ligating the small tributaries as well as the inferior pancreaticoduodenal artery. The dissection was carried through the pancreas on the left of the portal vein. The pancreatic duct was separately ligated. The pancreas was very fibrosed and indurated. Two mattress silk sutures were placed in the cut end of the pancreas. The duodenum was clamped in its third portion, divided and inverted with a Parker-Kerr stitch, reinforced with interrupted silk sutures. A Penrose sheath-drain was placed to the cut end of the pancreas. It was an easy operation, the patient stood the procedure well, and left the table in good condition.

Postoperative Course—The convalescence was uneventful until the seventh postoperative day, when what appeared to be a clean wound broke down. There was marked tryptic activity of the secretion and superficial suction was used. Four days later bile suddenly began to drain and continued for two weeks. Suction was maintained, the wound slowly healed and the patient was discharged on the fortieth postoperative day. He had a fair appetite and slowly gained weight on a low fat diet. He had no diarrhea or glycosuria but occasionally complained of transient, vague lower abdominal pains. He appeared to be doing well when he suddenly died, three months after operation. No postmortem examination was obtained.

Pathology Note—The tumor in the head of the pancreas was 2×3 cm in diameter and occluded both the pancreatic and common ducts. In and around the main tumor were numerous small cysts filled with clear yellow gelatinous material. The duodenal mucosa was not involved. Microscopically, the tumor was made up of cells varying in size and shape invading the stroma of the gland. Many of the cells were secreting mucus and some of the acini formed by the invading cells were filled with mucus. Some of the tumor cells were found invading the parenchyma of the regional lymph nodes by direct extension and by metastasis. *Pathologic Diagnosis*—Mucus secreting adenocarcinoma of the head of the pancreas, with metastases to local lymph nodes.

Comment—This patient had symptoms severe enough to bring him to the clinic one year before admission. Roentgenologic examination was advised but he did not return. Since there was a marked deformity of the duodenum on admission it is likely that a diagnosis could have been made earlier. He had severe liver damage, with a high icteric index and low protein previous to the first stage. His general condition was markedly better when the second stage was performed. The drain left in at the second operation undoubtedly contributed to the wound disruption, since there was active tryptic secretion in the wound. There was bile drainage and clay-colored stools for two weeks, indicating that the common duct may also have been digested in spite of a double ligation and transfixion with silk. Postoperatively, he had no glycosuria or diarrhea and was gaining weight. Cause of sudden death unknown. He had severe arteriosclerosis and mild decompensation. Lymphatic metastases were also found in the specimen.

Case 4—*History No B4275 H M, male, age 44. Admitted June 10, 1941. Three months—gaseous indigestion and constipation. Five weeks—dull epigastric pain and fullness. Ten days—lumbar pain. Two days—jaundice, ten pounds' weight loss. Two-stage operation. Cholecystojejunostomy, entero-enterostomy, resection duodenum and pancreas, gastrojejunostomy. Recovery. Living and well nine months.*

Chief Complaint—Jaundice

Present Illness—Thirteen weeks before admission he developed an upper respiratory infection accompanied by constipation. This was followed by a gradually increasing sensation of epigastric fulness, indigestion and belching, relieved by bisodol. All of these symptoms increased and were worse two hours after eating. Five weeks before admission he consulted his physician who made a tentative diagnosis of peptic ulcer and gave him a diet. His symptoms increased in severity, and ten days before admission he developed pain in the lumbar region at the same time as the epigastric fulness. Two days before entry he noted jaundice and clay-colored stools. During the past three weeks he had noticed increasing fatigue and had lost ten pounds' weight. *Family History*—Mother died of diabetes.

Physical Examination—Showed a heavy, well-nourished individual, not appearing acutely or chronically ill. There was a slight icteric tint to the skin, and the liver edge was just palpable below the costal margin. Otherwise negative.

Laboratory Data—Urine. Bile positive. Liver function (bromsulfalein) July 6, 1941—five minutes—45 per cent dye retention, 30 minutes—22 per cent dye retention. July 18, 1941—Blood fats. Serum titrated fatty acid 19.5 mg per cent per liter, serum lipid phosphorus 111 mg per cent, serum total cholesterol 245.0 mg per cent, serum unesterized cholesterol 72.0 mg per cent.

Roentgenologic Examination—This showed cardiac enlargement, calcified pulmonary tuberculosis and hilar lymph nodes, old pleurisy, left base. Duodenal loop wide, as if there were a tumor in the head of the pancreas. The lesser border was more smoothly outlined than the greater border of the curve, there was a question also of duodenal ulcer.

Operation—A W O. June 23, 1941. Cholecystojejunostomy, Entero-enterostomy. A right upper rectus incision was made, and the gallbladder and common duct were found to be greatly dilated. There was a firm mass, 4 cm in diameter, in the head of the pancreas in the region of the common duct medial to the second portion of the duodenum. The tumor was freely movable. There was some thickening in the pylorus suggesting an ulcer. The jejunum was divided and an end-to-side anastomosis was performed. The blind end was then anastomosed to the fundus of the gallbladder in the usual manner.

Postoperative Course was uneventful. His symptoms disappeared, his appetite improved, and the laboratory findings were all normal.

Second Operation—A W O July 21, 1941. Resection of the Duodenum and Head of the Pancreas with Posterior Gastrojejunostomy. A right rectus incision, excising the old scar, was made. The tumor was found to be reduced to almost half the size found at the previous operation. The peritoneum was incised along the lateral border of the duodenum which was reflected medially with the head of the pancreas. Considerable bleeding was encountered in this usually avascular area. A very liberal collateral circulation seemed to have been developed. The right gastric and gastroduodenal arteries were then ligated and the pyloric region was mobilized, clamped and divided. The jejunum was then brought up through the transverse mesocolon and a posterior gastro-



FIG. 1—Case 4. Air in the extrahepatic biliary passages.

jejunostomy was performed in the usual manner. The common duct was then divided and triply ligated with silk 0.5 cm apart, the distal suture transfixing the duct. Inadvertently, the intravenous therapy had failed to function properly and the patient went into shock. Since the most difficult part of the operation remained it was necessary to cease operating until his circulatory collapse had been corrected. The last portion of the duodenum was found to be tied down by adhesions and there was difficulty in freeing up this portion. This was further complicated by the fact that the patient was very obese and the mesentery to the small bowel greatly thickened. In order to get well around the tumor it was necessary to leave a very short stump of the duodenum for inversion. In retrospect, this part of the operation would have been much easier if the division had been made in the jejunum below the ligament of Treitz rather than in the duodenum. The dissection was then carried along the portal vein, ligating its tributaries and the inferior pancreaticoduodenal vessels. The body of the pancreas was unusually hard. The pan-

creatic duct, which was dilated and filled with secretion, was separately ligated. A partial V-excision transversely was used and the end of the pancreas closed with interrupted mattress sutures. The wound was closed in the usual manner with interrupted silk. A rubber sheath drain was placed to the cut surface of the pancreas.

Postoperative Course was complicated by a right lower and middle lobe atelectasis. However, following aspiration his vital signs were essentially normal on the second postoperative day and thereafter he had an uneventful convalescence. The fluid around the drains showed tryptic activity and continuous suction by a catheter was used. On the eleventh postoperative day bile appeared and the stools became clay-colored. Bile drainage ceased in five days. The wound healed well but there was intermittent pancreatic drainage for six weeks. He was discharged August 20, 1941.

Pathology Note—The cut surface of the tumor measured 2×3 cm in diameter. It obstructed both the common and pancreatic ducts to within 1 cm of the ampulla, which was not involved. There was atrophy and fibrosis of the normal pancreatic tissue. Several lymph nodes examined showed no metastasis. *Pathologic Diagnosis*—Adenocarcinoma of the head of the pancreas, Grade II.

Subsequent Course—The patient returned to work one month after leaving the hospital, and has continued ever since. He has been on a regular diet, and continued to gain weight, now being rather obese and weighing 175 pounds. He has had no glycosuria, diarrhea or other evidence of disturbed fat or carbohydrate metabolism. *Röntgenologic Examination*, December 5, 1941, shows a normally functioning gastro-intestinal tract, with the gallbladder and biliary tree filled with air (Fig 1). Liver shows no enlargement, March, 1942.

Comment—This patient had a short history and was in excellent condition. In retrospect, it is likely that a one-stage procedure could have been done successfully. On the seventh postoperative day there was digestion of the wound evident. Bile did not appear until the eleventh postoperative day and lasted only five days. The pancreatic fistula drained for five weeks. Postoperatively, the patient followed a routine diet on which he gained weight, and there were no gross abnormalities of digestion noted. Occasionally during the first two months postoperatively he had a mild attack of diarrhea. The technical procedure would have been much easier in this patient if the intestine had been divided at the ligament of Treitz rather than in the third portion of the duodenum. The patient was fat and the mesentery to the small bowel thick. These factors, plus the location of the tumor adjacent to the third portion of the duodenum, rendered mobilization of this portion of the duodenum difficult.

Case 5—History No 7023 A C, female, age 53. Admitted May 18, 1941. Six months—constipation. Four months—itching. Three months—jaundice, pain, fatigue, clay-colored stools, 20 pounds' weight loss. Marked hepatomegaly. Cholecystogastrotomy. Refused second operation until three months later. Resection duodenum and pancreas, gastropylorostomy. Operative death—acute yellow atrophy of liver.

Chief Complaint—Itching.

Present Illness—In November, 1940, for the first time she became constipated and this persisted until the character of the stool changed in February, 1941. Early in January she developed itching over the entire body, worse on the extremities. She consulted different doctors and received various lotions and was once told she had scabies. She noted her skin was rather dark but it was not until February that it became yellow. At this time she became easily fatigued and lost her appetite. She shortly developed a sensation "as though the stomach were pressing on the back bone," food was disagreeable

and she frequently vomited. Epigastric pain appeared which was relieved by leaning forward. She also developed a lower abdominal cramping pain preceding bowel movements and relieved by them. She had lost 20 pounds' weight.

Past History—Irrelevant except for hypertension of four years' duration.

Physical Examination—The patient was a small, emaciated woman appearing chronically ill. Her skin was markedly jaundiced, having a peculiar dark bronze color, and there were numerous excoriations on the trunk and extremities. Tongue was heavily coated. The abdomen was slightly distended, the epigastrium very tender, and the liver enlarged to a hand's breadth below the costal margin.

Laboratory Data—Blood RBC 4.2, hemoglobin 80 per cent, WBC and smear normal. Urine Negative except for strongly positive bile. Stool Guaiac and bile negative. Serum proteins 6.9 mg per cent, serum albumin 3.74 mg per cent, serum globulin 3.25 mg per cent, icteric index 95 units. Liver function test 227 per cent sodium benzoate excreted in one hour as hippuric acid. Van den Bergh qualitative direct negative, indirect, 8.75 mg per cent. Gastric analysis 4 cc free HCl.

Roentgenograms negative except for displacement of stomach laterally and posteriorly because of questionable enlargement of liver.

Operation—A W O June 2, 1941. Exploratory Celiotomy, Cholecystogastrostomy. The liver was found enlarged to the iliac crest and had a dark purple color, with a pebbled surface. The gallbladder and common duct were markedly dilated. There was a mass 3 cm in diameter in the region of the common duct behind the second portion of the duodenum and in the pancreas. There was considerable edema and numerous dilated vessels. Some time was consumed in dissection and trying to decide whether this was a stone in the common duct or a tumor. An unsuccessful biopsy was attempted. Finally a cholecystogastrostomy was performed.

Postoperative Course—Uneventful. The icteric index quickly fell to normal and the itching promptly ceased. The jaundice slowly faded, her appetite returned and symptoms disappeared. She felt so well that she refused further operative treatment and was discharged June 23, 1941. She continued to improve at home, gaining weight to 90 pounds. She had never weighed over 100 pounds. She wished to continue her dog farm during the profitable season but was finally persuaded to return to the hospital on August 24, 1941. In the meantime she had shown no free hydrochloric acid fasting but 16 units after histamine. Bromsulfalein liver function, 25 per cent dye retention in seven minutes, and no dye retention at 30 minutes. Icteric index 3.

Second Operation—A W O August 28, 1941. Resection Duodenum and Pancreas, Gastrojejunostomy, posterior. An upper right rectus paramedian incision was made. The liver was still enlarged to four fingers below the costal margin. The tumor, instead of being smaller as in previous cases, had enlarged to 6 cm in diameter. The first impression was that it was inoperable but as the dissection was begun it seemed that there was some possibility that it might be removed. The peritoneum was incised along the lateral surface of the duodenum which was turned up with the head of the pancreas. The right gastric and gastroduodenal vessels were ligated, the pylorus clamped and divided. The dissection was then carried along the inferior portion of the duodenum, entering the free peritoneal cavity at the ligament of Treitz. A specially devised curved clamp was then carried under the vessels of the mesentery. The transverse colon was then reflected upward exposing the ligament of Treitz, and the clamp which was placed on the proximal jejunum. A Peyer clamp (Fig 2) was placed just distal to this and the jejunum divided and inverted. The usual posterior gastrojejunostomy was performed. The dissection was then carried along the portal vein ligating the tributaries. The tumor was found tightly adherent to the wall of the portal vein, which at one point was entered but readily repaired. The remainder of the dissection proceeded without incident. The patient had had a stormy anesthesia and it was necessary to resort to drop-ether. However, she stood the operation quite well. At the completion her systolic blood pressure was 100-110, and pulse 90.

CARCINOMA OF PANCREAS

Postoperative Course—This patient never regained consciousness in spite of all supportive measures. She became rapidly and deeply jaundiced, and died within 48 hours. Sections of the liver showed typical acute yellow atrophy.

Comment—There was undue delay in the diagnosis of this patient, and the primary liver damage was severe. A cholecystogastrostomy was performed at the first stage as being the simplest means of relieving the biliary obstruction in a critically ill patient. The optimal time for the second stage was missed owing to the patient's refusal. This situation, in itself, may be used as an argument for a one-stage procedure. When the second stage was attempted in this patient the tumor was larger than it was at the time of the

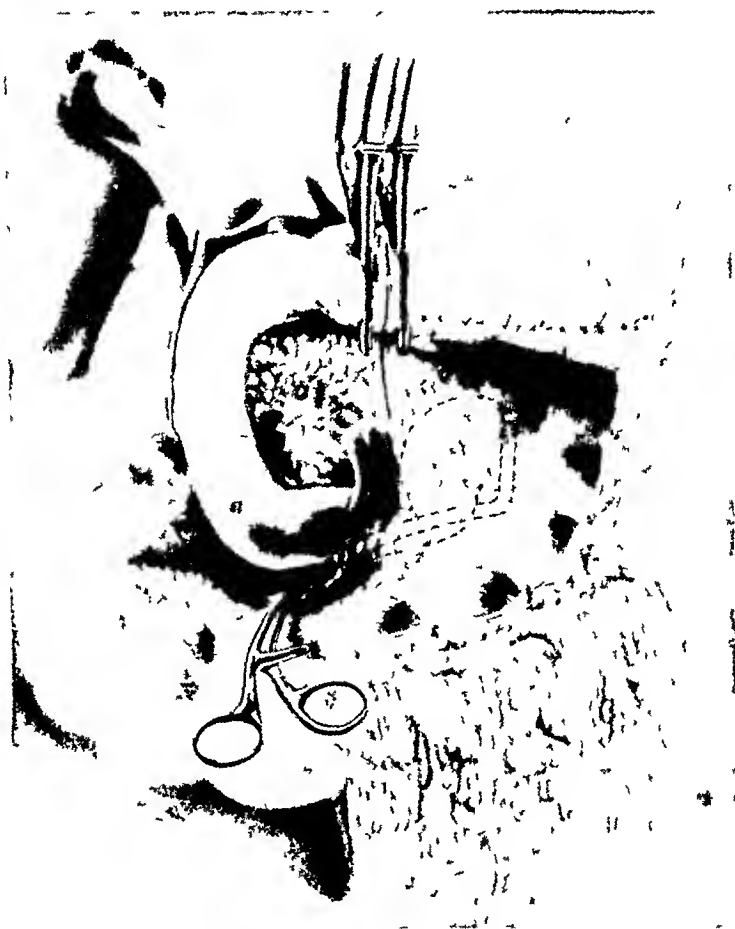


FIG. 2—Case 5. A special clamp is used for division of the jejunum.

first operation, whereas in all the other two-stage procedures the tumor was smaller at the second operation than when seen at the first stage. In retrospect, this patient must also be considered as inoperable owing to extension of the tumor involving the portal vein, although this could not be determined without dissection of this area. Also, in retrospect, an unwise attempt was made to perform a radical removal of the tumor. She developed a typical syndrome of acute yellow atrophy of the liver, proven histologically. The cause of this is unknown but it is possible that a heavy ether anesthesia, in the presence of an already damaged liver, may have contributed to the fatal outcome.

Case 6—*History No B17187 V A, female, age 50 Admitted June 30, 1941 Three months—voluminous, frothy offensive stools, two months—anorexia and cramps preceding defecation, one month—red scaly eruption on hands and ankles, fissures at corner of mouth, 30 pounds' weight loss, five days—jaundice, glycosuria One-stage resection duodenum and pancreas, cholecystojejunostomy, posterior gastro-enterostomy Recovery Diarrhea, diabetes and weakness persist but no evidence of recurrence Avitaminosis Still living nine months*

Chief Complaint—Voluminous stools

Present Illness—Began three months before admission when one morning she passed a large malodorous, foamy, light-colored stool During this morning she had three such stools and since that time she had had two to four similar bowel movements each day Shortly after this she was placed on a bland diet without added vitamins and remained on this until admission During this period she had had no pain except for a crampy generalized abdominal ache before defecation Her appetite was poor and she had lost 30 pounds of weight During the month preceding admission a dry, scaly, reddened eruption appeared on the dorsum of the hands and ankles and fissures developed about the corners of the mouth She had never been jaundiced and stated that she did not have diabetes *Past history and family history* irrelevant

Physical Examination—The patient was an emaciated woman, appearing chronically ill There were scaly, erythematous, desquamating lesions on the ankles and dorsum of the hands The corners of the mouth showed many fine fissures The liver edge was palpable two fingers' breadth below the costal margin A stony-hard 4 cm-mass, which moved slightly with inspiration, was palpable in the right upper quadrant, just to the right of the midline

Laboratory Data—Blood RBC 37, hemoglobin 78 per cent White count and smear normal Urine Albumin +, sugar 4+, acetone 2+ Stools were light greenish-brown, soft, semifformed, bile negative Some specimens were guaiac positive and others negative Icteric index 8 Fasting blood sugar 159 mg per cent NPN 18 mg per cent Prothrombin time 28 per cent of normal Gastric analysis Free HCl—65 units After histamine, free HCl—76 units Serum albumin 3.95 gm per cent, Serum globulin 1.90 gm per cent, Calcium 9.91 gm per cent, Phosphorus 2.22 gm per cent, Liver function (bromsulfalein 5 mg per Kg) 5 minutes—90 per cent retention, 30 minutes—60 per cent retention

Röntgenologic Examination—Gastro-intestinal series negative Cholecystogram showed 50 per cent dye retention in 30 minutes, with nonvisualization of the gallbladder

On the ninth day after admission she became jaundiced, the icteric index was then 35, and the direct Van den Bergh positive During this preoperative period the patient was on a calculated diabetic diet containing protein 120 Gm, fat 50 Gm, with added calcium, viosterol and nicotinic acid The insulin requirement varied from 20 to 50 units per day

Operation—SCH July 12, 1941 Retrocolic Cholecystojejunostomy, Posterior Gastrojejunostomy, Resection of Duodenum and Pancreas An upper right rectus incision was made The liver was normal in appearance but the gallbladder and common duct were markedly dilated A hard, nodular mass, grossly carcinoma, was seen in the head of the pancreas It was decided to perform the resection in stages in order that the operation might be terminated promptly if the patient's condition did not remain satisfactory A retrocolic cholecystojejunostomy 40 cm below the ligament of Treitz was carried out as a first stage The pyloric end of the stomach was mobilized and divided and a posterior gastrojejunostomy was done, the proximal jejunum being utilized In this manner the second stage of the operation was completed The common duct was divided, ligated and transfixed with silk The pancreaticoduodenal artery was ligated in continuity and divided The first and second portions of the duodenum, together with the head of the pancreas, were then mobilized laterally, the pancreas was divided between clamps at the level of the superior mesenteric vein with preservation of the superior

mesenteric vessels The inferior pancreaticoduodenal artery and the pancreatic branches of the superior mesenteric vein were then ligated, following which the duodenum and tumor mass were retracted to the right and the duodenum divided just proximal to the ligament of Treitz The entire duodenum and tumor mass were then removed *en bloc* and the distal duodenal stump closed The remaining portion of the pancreas to the left of the superior mesenteric vessels was then resected well out to the tail, leaving about 2-3 cm of attenuated pancreas The wound was closed in the usual manner with interrupted silk A slip drain was placed beneath the anterior rectus fascia but not into the peritoneal cavity

Pathology Notes—The tumor had completely closed the pancreatic duct but the common duct was still partially patent Atrophic changes in the pancreatic tissue were marked Diagnosis was adenocarcinoma of the head of the pancreas with secondary fibrosis and atrophy of the acini of the body and tail, metastases to the local lymph nodes

Postoperative Course—The patient made an uneventful recovery from the operation, the slip drain was removed in 48 hours, and the wound healed *per primam*, without evidence of a pancreatic fistula The blood sugar on the morning of the first postoperative day was 126 mg per cent After the immediate postoperative period, and when peristalsis had returned, the patient was placed on a high protein, low fat, high carbohydrate diet with added vitamins, including vitamin K Viosterol and calcium were given by mouth The stools were dark brown, semiformal and guaiac negative, the prothrombin time normal The bromsulfalein test (July 31, 1941) showed no retention at the end of 30 minutes In the serum the titrated fatty acids were 80 mg per cent per liter, the total cholesterol 123 mg per cent, the unesterized cholesterol 40 mg per cent, and the serum proteins 4.41 Gm per cent With the improvement in liver function there was a marked increase in the severity of the diabetes, and the insulin requirement was from 70 to 120 units per day There were several episodes of diarrhea with bulky stools, which responded poorly to pancreatin by mouth By the time a satisfactory lipocac preparation could be obtained the patient was ready for discharge and this preparation was not given during her hospital stay She was discharged from the hospital, August 16, 1941, 35 days after operation

She was readmitted to the hospital, September 7, 1941, with a severe diabetes, acidosis and dehydration Blood sugar was 329 mg per cent She was discharged, October 3, 1941, asymptomatic

Since then there have been frequent attacks of diarrhea and steatorrhea, aggravation of the diabetes, some nausea and occasional vomiting There have been marked weakness and a failure to regain the lost weight A gastro-intestinal series has shown the gastrojejunostomy stoma to be patent A bromsulfalein test (2 mg per Kg and, therefore, not comparable with the previous test) showed a 48 per cent retention of the dye at the end of 30 minutes This was done December 30, 1941 The patient has subsequently shown evidence of multiple vitamin deficiencies and is at present in the hospital under treatment for this condition The liver is readily felt and descends two to three fingers' breadth below the costal margin This represents some enlargement since the pancreatectomy On February 14, 1942, serum titrated fatty acids were 146 mg per cent, and cholesterol 220 mg per cent Icteric index, March 20, 1942, increased to 40 The patient is now under treatment with lipocac

Comment—This patient, in spite of a severe avitaminosis and diabetes, had an unusually smooth convalescence following a one-stage operation, without drainage She did not have a pancreatic fistula, although only a very small amount of functioning pancreatic tissue remained She is the only one of the six patients reported who presented the classical symptoms of voluminous, frothy, offensive stools usually associated with pancreatic deficiency She is also the only one complicated by a severe and persistent diabetes

She had, and still has, multiple vitamin deficiencies. It is not yet determined how much of her present difficulty is due to a food and vitamin deficiency and how much may be contributed by a lack of the external secretions of the pancreas.

DISCUSSION

Since cancer of the pancreas and ampullary region was fully discussed before this society last year by Hunt,⁵ Schnedorf and Orr,⁷ Whipple,⁹ and others, we will limit the discussion in this paper to points illustrated by the cases presented. Cancer of the pancreas and ampullary region may well be considered as an entity since it is frequently impossible clinically to determine the exact site of origin. Furthermore, the extension of strictly ampullary tumors makes it necessary for one dealing with this problem to be familiar with, and capable of executing the radical excision of the duodenum and pancreas.

Reports on cancer of the pancreas are frequently pessimistic, and cite, as a basis for this pessimism, the short duration of symptoms and rapidly fatal course of the disease. It should be recalled, and history reveals, that this attitude prevails when cancer of an internal organ is first attacked therapeutically. Beik¹ has shown, in a review of the literature, that the average duration of symptoms from the onset of the disease to admission to the hospital is six months, with extremes of approximately four to ten months. This delay offers considerable hope that in the future, as the symptoms of the disease become more clearly recognized and the value of the radical surgery more definitely established, more optimism regarding cancer of the pancreas will be justified.

Symptoms. Beik¹ has recently surveyed the literature, with particular reference to symptoms and diagnosis. He states "In many cases the disease is incorrectly diagnosed and its presence is missed in the early stages because in the mind of the average physician certain impressions of traditional diagnostic criteria have persisted despite the fact that they have been repeatedly shown to be false." He found, by a poll of recent graduates, that 92 per cent of them considered painless jaundice the most important symptom. On the contrary, a survey of the literature revealed that pain was one of the most common symptoms. Both as an initial symptom and as a chief complaint, it was found in approximately half the cases, whereas sometime during the course of the disease pain was found in 76 per cent of all patients.

The type of pain cannot be said to be characteristic (Cases 1, 2, 3, 4 and 5). Pain such as is illustrated in Case 1 is most characteristic. It is severe, and frequently described as though the stomach were pressing on the back bone, and is worse on reclining. It is frequently relieved by relaxing the abdomen or standing up.

Jaundice, as an initial symptom or chief complaint, is less frequent than pain (Cases 1, 3, 4, and 6). It is obvious that the location and extent of the tumor determine the symptoms. Since the cancer is located in the head of the

pancreas in 92 per cent of the patients who came to operation and in 72 per cent of those at necropsy, jaundice sometime during the course of the disease is a common symptom. Either the common or pancreatic duct or both may be involved. Even when the cancer arises in the ampulla, one or the other of these ducts may remain patent. In Case 2 the tumor of the ampulla completely blocked the common duct, whereas the pancreatic duct remained patent. Brunschwig reported a similar tumor the same year, treated in the same manner, in which only the pancreatic duct was blocked. It should be emphasized that while painless jaundice should lead one to suspect cancer of the head of the pancreas, this syndrome is found in only 18 per cent of all patients with such tumors. It was found in only one patient in this series.

A palpable liver or gallbladder is frequently cited as of diagnostic significance. The enlargement of these organs appears to depend chiefly on the degree and duration of the obstruction of the common duct. An enlarged liver is more frequently noted than an enlarged gallbladder. Considering all the cases with jaundice in the literature, only half have had a palpable gallbladder. Even though the common duct is completely obstructed, with jaundice present, but for a short time (Cases 2 and 4), the liver and gallbladder may not have had time to enlarge.

Weight loss is frequently profound and rapid. Beik found it to average 26 pounds, or 6.8 pounds per week, and it was present in 87 per cent of all patients. Fatigue and weakness, as well as nausea or vomiting, are also frequent symptoms. Carcinoma of the pancreas is frequently thought to be associated with voluminous, foul, frothy diarrhea. This is not a frequent occurrence, and was found in only one of the six cases reported. Beik¹ found diarrhea reported in only 11 per cent of the cases in the literature. It is not clear why some patients have the typical fatty diarrheal stool and others, with a similar lesion, have no obvious abnormality of fat metabolism. The one patient in this series (Case 6) who manifested such a diarrhea also had a severe avitaminosis. She also had less functional pancreatic tissue remaining.

Laboratory Data—The roentgenographic findings are variable and frequently disappointing, particularly when the tumor is still in the operable stage. Positive roentgenographic findings are reported in the literature of 37 per cent of all cases. However, many of these were inoperable. Roentgenograms may demonstrate (1) Obstruction of the duodenum, (2) irregularity or encroachment on the duodenum, or (3) widening of the duodenal loop. Occasionally a large tumor of the tail or body of the pancreas may be seen pressing on the stomach. A negative roentgenogram has no significance in the diagnosis of cancer of the pancreas or ampullary region (Cases 1, 2, 4 and 6).

Laboratory findings are variable in the presence of carcinoma of the pancreas. Disturbances of fat and carbohydrate metabolism might be expected, depending on the location, extent and duration of the tumor.

Glycosuria has been reported in the literature in 10 per cent of all patients

with cancer of the pancreas. In different reports the frequency of this finding varies from 2 to 26 per cent. Likewise, hyperglycemia was found in 20 per cent of all patients, with a spread of 9 to 57 per cent in different reports. The more recent reports have a tendency to recognize a higher incidence of disturbed carbohydrate metabolism, probably because of more and better laboratory work. The glucose tolerance test presents a similar variability. Ranson, in 1935, found an impaired glucose tolerance in only one of 16 cases (6.2 per cent) whereas Berk found seven of nine patients (77.8 per cent) showed a positive test. The glucose tolerance test appears to be indicated in all suspected cases, since it has yielded valuable information when neither glycosuria nor hyperglycemia has been present.

In this series, Case 1 gave a history of glycosuria. However, on admission his fasting blood sugar was 79 mg per cent and a few days later it was 130 mg per cent. He showed no glycosuria while in the hospital. After 50 Gm of glucose his blood sugar rose to a high of 128 mg per cent in two hours. After a subtotal resection of his pancreas, leaving only a small ribbon 1 cm wide on the head of the pancreas along the duodenum, he still did not show glycosuria. Case 6 showed a persistent 4+ glycosuria unless controlled by insulin or diet. Preoperative fasting blood sugar was 159 mg per cent. Following operation the glycosuria fluctuated according to the diarrhea, being less when the diarrhea was greatest. On one occasion, following operation, she was admitted to the hospital with severe diabetes, acidosis and dehydration. None of the other patients gave evidence of disturbed carbohydrate metabolism.

There are a number of experimental observations which may be cited to explain the variable response of depancreatized patients. It is well known that pancreatectomy in different species of animals results in different degrees of disturbed carbohydrate metabolism. There is evidence that this is in part due to the different activity of the pituitary and adrenal glands. In man the high incidence of glycosuria in acromegalic persons is circumstantial evidence. Thus, as stated by Best: "The diabetic state, therefore, may not be due primarily to subnormal secretion of antidiabetic hormone but to various other hormonal disturbances, especially of the pituitary and adrenals." It may be added that the thyroid also plays an indirect rôle. In support of this we may cite one patient who was suffering from acromegaly, hyperthyroidism and severe diabetes. Following thyroidectomy the patient's previously high insulin requirement was reduced to a low level. It is also possible that the part of the pancreas removed may be a determining factor. It is known that in the dog different parts of the pancreas contain different amounts of the antidiabetic factor (splenic end 4, middle 3, and duodenal end 2 units per Gm). A history of preceding diabetes or a family history of diabetes may be obtained, as in Case 4. McKettrick and Root found carcinoma of the pancreas comprised 32.4 per cent of all malignant conditions with a history of diabetes. Others have maintained that a preceding history of diabetes is incidental.

The evidence for deranged fat metabolism also presents a similar variability. There are now a number of living patients who have survived a subtotal pancreatectomy, and who have had no obvious evidence of disturbed fat metabolism. In some of these patients there seems to be no doubt that the external secretions of the pancreas do not reach the intestines. One may, therefore, infer that the external secretions of the pancreas are not essential to life or that their functions may be taken over by other portions of the gastro-intestinal tract in some patients.

Various methods of determining faulty fat metabolism in cancer of the pancreas have been tried but the results have usually been disappointing. This may have been due to the fact that cancer of this organ does not produce a constant clinical syndrome nor result in uniform pathologic changes in the pancreas. Serum lipase determinations appear to hold considerable promise as a diagnostic test. Various authors have found that the serum lipase is elevated in a high percentage of cases of pancreatitis. However, Comfort and Osterberg found increased values in only 40.5 per cent of 69 cases of carcinoma of the pancreas. One may conclude that the absence of evidence indicating disturbed fat metabolism is of no significance in the diagnosis of cancer of the pancreas. However, a search should be made for evidence of disturbed carbohydrate or fat metabolism as its presence in conjunction with other findings may be of help.

Surgical Treatment—The preoperative treatment of patients with cancer of the pancreas involves the same principles as does cancer of the stomach or extrahepatic bile ducts. An attempt should be made to restore the physiology of the patient to as nearly normal as possible. The causes of death, as recorded by Hunt, in operations for periampullary cancer, in the order of frequency, are hemorrhage, peritonitis, duodenal fistula, shock and pneumonia. Most of these problems have been solved by the use of vitamin K in the jaundiced patient, hydrochloric acid for the infected stomach with low acidity, improved surgical technique, adequate use of intravenous fluids, blood and plasma, the use of chemotherapy, adequate parenteral vitamins, and improved anesthesia. With these considerations in mind, there is already reason to suppose that the operative mortality in experienced hands will not exceed 10 to 15 per cent.

The technique of the operation, whether it shall be local or radical, one-stage or two-stage, and the treatment of the bile and pancreatic ducts, has been not yet clearly established. The more formidable radical operation for cancer of the ampulla has been frequently avoided in the past. Several of these patients, reported in the literature, having a local excision have had a recurrence. It is reasonable to suppose that in some of these a more radical excision might have resulted in a cure. Case 2 is a successful result to date (two years, nine months), but a local operation of this type cannot be considered an ideal operation for cancer, and the surgeon who approaches one of these tumors should be prepared to perform the radical operation if indicated.

The advantages of the one- and two-stage operations have been discussed

by Whipple. Evidence is accumulating that the one-stage operation may be the procedure of choice. The operative mortality of the one- and two-stage operation, as reported, is about equal, although the numbers reported appear to be too few to enable one to draw final conclusions. There are undoubted and obvious advantages in a radical removal of the tumor at one operation, and it is to be hoped that this will be possible as more patients are diagnosed in the earlier and more favorable stages of the disease. However, it is likely that a two-stage operation may still be indicated in some patients, and the problem is raised as to when this is necessary. If the cancer is localized in the tail of the pancreas and removal of the duodenum is unnecessary, there is no indication for a two-stage operation (Case 1). There is also no indication for a two-stage operation in the rare patient with a small cancer of the ampulla which can be excised with an adequate margin and the ducts reimplanted (Case 2). The radical excision of the duodenum and pancreas with a cholecystojejunostomy and gastrojejunostomy, would not seem to be contraindicated if the liver has not been seriously damaged and the patient is in otherwise good condition. In retrospect, it would seem as though Case 4 might have been safely concluded in one operation rather than two. However, it is frequently difficult to determine before operation how well a patient will stand such a long and arduous procedure (Cases 3, 5 and 6). The operation described in Case 6 illustrates a method whereby the procedure may be terminated at any of three stages if the patient is not doing well, or it may be completed in one operation as in this case. One of the chief disadvantages of the two-stage operation is illustrated by Case 5. The long-standing jaundice and evident liver damage appeared to indicate the advantage of a two-stage operation. Furthermore, considerable time had been consumed in an effort to determine whether the patient had a cancer or a common duct stone. She withstood the procedure well, under cyclopropane anesthesia, and it is likely she would have withstood a radical excision equally well. Following this she felt so well that she refused the second operation until nearly three months later. She then appeared to be in much better general condition. However, she took a poor anesthesia, requiring drop-ether, the tumor had increased in size, and was followed by acute yellow atrophy of the liver, and a fatality.

Biliary and pancreatic fistulae have been one of the annoying complications of operations for cancer of the pancreas. Two patients in this series had biliary and pancreatic fistulae, and both were two-stage operations (Cases 3 and 4). In both patients the biliary fistula appeared several days after the pancreatic secretions appeared. The pancreatic secretions possessed marked tryptic activity, suggesting that this may have been a factor in digesting the common duct closure. In both patients the common duct was ligated with silk at the second operation. It is possible that the biliary fistulae could have been avoided by ligation and division of the common duct at the first operation, before the pancreatic secretions were freed. Both of these patients had drains placed to the cut surface of the pancreas. Since the one-stage

operations (Cases 1 and 6) were not drained, one might assume that this was responsible for the fistulae. However, both of these patients had little indication for drainage since, in Case 1, the ducts draining the remaining pancreas were still intact, and in Case 6, only a very small amount of the atrophic tail of the pancreas remained. In Cases 3 and 4 the ducts were filled with secretion at the time of operation and more secreting pancreas remained *in situ*.

Some surgeons have anastomosed the jejunum to the common duct, which may be preferable to the cholecystojejunostomy. Leakage from the ligated common duct might thus be avoided. The cholecystogastrostomy appears to have fallen into disrepute owing to constriction of the stoma and the fact that it is frequently followed by subsequent liver damage. Data is not available as to whether this liver damage may occur only in those patients with an infected gastric content owing to absence of hydrochloric acid. It is worthy of note that all patients with a cholecystojejunostomy have shown air throughout the biliary tree, indicating the possibility of ascending infection by this route likewise.

TABLE I
RÉSUMÉ OF CLINICAL DATA

Case	1	2	3	4	5	6	Average in Literature*
Pain	+	0	+	+	+	0	50†-76%
Jaundice	0	+	+	+	+	0	22†-60%
Pounds weight loss	15	26	20	10	20	30	87% Av 26 lbs
Fatigue and weakness	+	+	+	+	+	+	51%
Nausea or vom- iting	+	0	+	+	+	+	42%
Diarrhea	0	0	0	0	0	+	11%
Glycosuria	+	0	0	0	0	+	10%
Location of tumor	Body	Ampulla	Head	Head	Head	Head and body	82% of all cases in head
Operation	Resection spleen and pan only	Resection tumor trans- duodenal	Resection duod and pan 2 stages	Resection duod and pan 2 stages	Resection duod and pan 2 stages	Resection duod and pan 1 stage	
Results	Died 5 mos postop with met- astasis	Living and well, 2 yrs and 8 mos	Died sud- denly 3 mos postop	Living and well, 9 mos	Op death, acute yel- low atrophy	Living, 9 mos	

* Berk, J. Edward¹

† Initial symptom only

The postoperative care of patients following a radical resection of the pancreas is not clearly established. It appears that only a very small amount of pancreas is necessary to prevent diabetes. It appeared in only one patient in this series, and was present before operation (Case 6). It also appears that in some patients the external secretions of the pancreas are not essential to life. If further experience should prove that the external secretions are essential in some patients, then some satisfactory method of anastomosing

the pancreatic ducts to the intestine must be developed. More observations and a careful follow-up will be needed to determine whether such changes as a fatty infiltration of the liver will occur. The nature of lipocaic and how it prevents fatty infiltration of the liver is not clear. Recent observations indicate that lipocaic, pancreas, rice polishings and yeast contain a dietary factor which prevents this liver damage. Hence, it may be found that a patient with a normal liver and an adequate diet may require no supplementary therapy (Case 4). It appears that most of the known enzymatic functions of the external secretions of the pancreas may be performed to a greater or less extent by some other portion of the gastro-intestinal tract.

SUMMARY AND CONCLUSION

(1) Six patients with cancer of the pancreas and ampullary region are reported.

(2) There was one local excision of cancer of the ampullary region and five radical operations, with one fatality (16.6 per cent).

(3) There were four radical excisions of the duodenum and pancreas.

(4) Three of the six patients are still living, one of whom has symptoms of disturbed carbohydrate and fat metabolism.

(5) The external secretions of the pancreas in some patients do not appear to be essential to life.

(6) Earlier diagnosis of more patients with cancer of the pancreas, still in the operable stage, is possible. The radical excision of the tumor is also possible, with a comparatively low mortality. More observations and follow-up reports on patients having these operations are needed.

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DISCUSSION—DR ALLEN O WHIPPLE (New York, N Y.) The remarks that Doctor Churchill made this morning in regard to the radical procedures for carcinomata of the lower end of the esophagus and of the cardia, apply very aptly to this operation for carcinoma of the pancreas in the ampullary region of the duodenum The operation is unquestionably in an experimental stage That is obvious from the study of the cases that have been reported recently

Doctor Harvey and Doctor Oughterson were among the members of this society who very kindly sent to me the reports of their cases, and I wish to express my appreciation to the members of the Association for this courtesy, whether they were published or not I certainly would appreciate others doing so

During the past year some 23 radical operations with removal of the duodenum and the head, or more of the pancreas have been reported in the literature or have been reported to me by surgeons here and abroad, bringing the total number of these operations since 1935 to 64 As a result of the introduction of three factors, vitamin K, the newer methods of preventing and combating shock, and the sulfonamide compounds, there is a very definite and fully justified trend toward the one-stage operation, as shown in increasing statistics

TABLE I
RÉSUMÉ OF 64 CASES OF RADICAL PANCREATODUODENECTOMY OPERATIONS
Collected to April 1, 1942

	Two-Stage	Postop Deaths	One Stage	Postop Deaths	Fistulae		
					D	B	P
Carcinoma of the ampulla . . .	15	2	6	2	—	6	8
Carcinoma of the pancreas	21	9	6	2	2	5	5
Carcinoma of the duodenum	2	1	7	2	—	—	2
Carcinoma of the common duct	3	0	2	2	—	1	2
Sarcoma of the duodenum	0	0	1	0	—	—	—
Chronic pancreatitis	0	0	1	0	—	—	1
Totals	41	12	23	8	2	12	18
Total operated cases				64			
Postoperative deaths				20			
Two stage		12		29	2%		
One stage		8		34	7%		

From my own experience, I am convinced that the one-stage operation, aside from saving the patient two anesthetics, two operations, and very often a very unfortunate delay between the first and second stage, as Doctor Oughterson mentioned, avoids the risk, or largely decreases the risk, of the biliary fistula from ligation of the cut end of the common duct by the immediate anastomosis of the common duct to the loop of duodenum

This is a real advance in the technic and result of the operation

Dr Herman Pearse has recently used the distal jejunal end to anastomose the gall-bladder proximal to gastrogastrostomy

About a month ago I carried out a very extensive one-stage resection of the antrum of the stomach, all of the duodenum, and to some extent the jejunum, together with all the head of the pancreas, uniting the cut end of the jejunum to the cut end of the common duct, approximately to the site of gastrogastrostomy This patient *did* develop a pancreatic fistula, but that is now closing

The problem of what to do with the stump of the pancreas is still unsolved I have performed a pancreaticoduodenostomy, in which the distal end of the pancreas was implanted into the distal portion of the duodenum in two patients, according to the scheme as first carried out by Koch in 1912 One of these patients has done exceedingly well, but the other patient developed a duodenal fistula, and on the tenth day had a very severe secondary hemorrhage which resulted in his death

We do not know as yet how essential the external secretion of the pancreas is in the metabolism of fat and its relation to fatty changes in the liver. We have observed three patients who have gone two years or more after total exclusion of pancreatic juice from the tract. Two of these patients were able to digest 80 to 85 per cent of manufactured

FIG 1 A

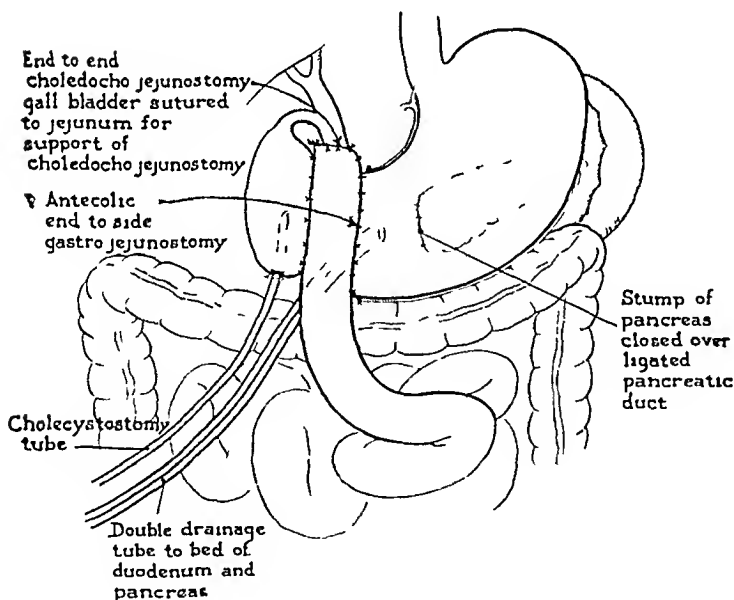
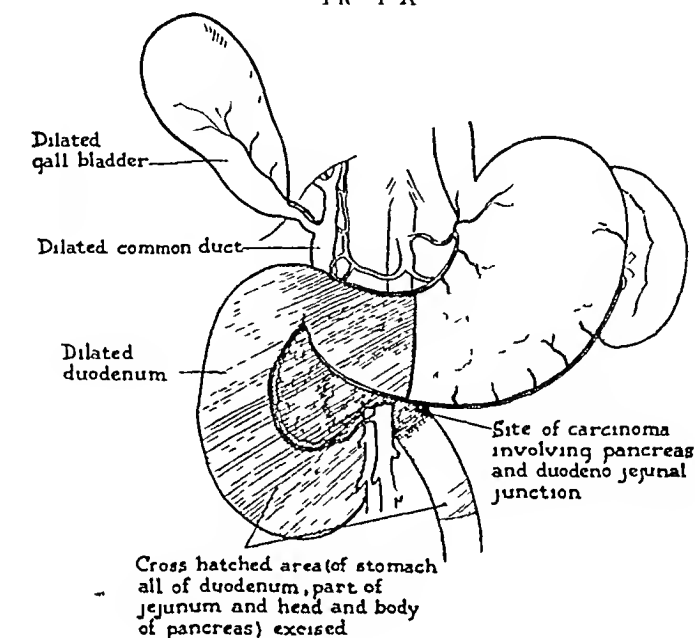


FIG 1 B

fat intake whereas one has shown 40 per cent fat residue in the stools. I think the reason for that is because we removed so much of the pancreas very much as in the case Doctor Oughterson reported. I believe that Doctor Dragstedt will be able shortly to give a definite opinion on this controversial question.

(Slide) This is a resume of the total number of cases reported in the literature or reported to me with a mortality of 12 or 29.2 per cent in two stage procedures and a mortality of 8 or 34.7 per cent in one stage procedures.

CARCINOMA OF PANCREAS

In my own case I have carried out four two stage operations with two deaths and six one-stage operations with four deaths
(Slide) This was an extensive removal of the stomach of the duodenum, and a large carcinoma of the jejunum This is the patient in whom I transplanted the head of the pancreas into the stump of the duodenum
(Slide) This is the antrum of the stomach pylorus and all the duodenum and some ten or 12 cm of the jejunum with the head of the pancreas
(Slide) This shows the amount of tissue removed the tumor being located here The next slide shows the procedure which we carried out and which saved an inversion brought the jejunum just to the point where it was resected anastomosed the stomach and implanted at the upper end the stump of the common duct That patient has not had a biliary fistula and has done better than the average I placed a tube in the gallbladder because it seemed to be rather tender and dilated
I again wish to state that the procedure is in the experimental stage and that, like the operations that Doctor Churchill discussed this morning it requires a great deal of further study and follow-up

DR THOMAS C ORR (Kansas City Kans) Two patients reported earlier are still living 23 months and 12 months following the operation Both were operated

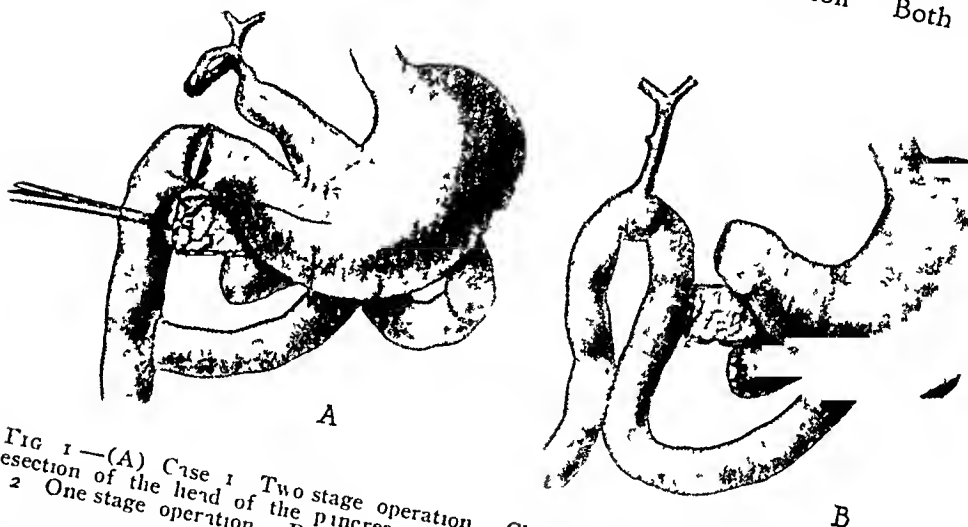


FIG 1—(A) Case 1 Two stage operation Cholecystogastrostomy followed in 117 days by resection of the head of the pancreas Neck of pancreas anastomosed to jejunum (B) Case 2 One stage operation Pancreas and common bile duct anastomosed to a jejunal loop

upon by the method described by Whipple Parsons and Mullins The following two cases have not previously been reported
Case 1—Female age 65 was operated upon for carcinoma of the head of the pancreas in two stages A cholecystogastrostomy was done September 11, 1941, and the duodenum and head of the pancreas were resected January 6, 1942 The stump of the pancreas was anastomosed to the jejunum (Fig 1 A) The abdominal wound healed promptly after the second operation and the patient left the hospital in 14 days The pathologist's diagnosis was early adenocarcinoma of the pancreas arising from the ductal structures At present April 1, 1942 her condition is satisfactory
Case 2—Male age 56 On April 28, 1939 the gallbladder was removed and the common duct was drained There were no stones found in either the gallbladder or head of the pancreas and duodenum were resected in one stage December 24, 1941 The severed end of the pancreas was anastomosed to the jejunum (Fig 1 B) There was some serous discharge from the wound but no evidence of pancreatic secretion He left the hospital in 31 days The pathologist reported a large ulcerating adenocarcinoma of the head of the pancreas with metastases to the regional lymph nodes tumor probably arose from the parenchyma of the pancreas A report received April 1, 1942 states that his condition is very good

DR J SHELTON HORSLEY (Richmond Va) The physiologists, Doctor Whipple, and Doctor Brunschwig and others have shown, very definitely, that the external secretion of the pancreas through the pancreatic duct is not necessary to life. However, like the old jingle that poverty is no disgrace, it certainly might be claimed that it is sometimes inconvenient. The methods of making these observations are probably not entirely fully settled, and it certainly is convenient to have the external secretion preserved if it can be accomplished. Of course, in most instances the lesions are so extensive that this cannot be done.

(Slide) I want to again report one case that has been reported previously. It is a case that I have mulled through because the diagnosis was not accurate preoperatively. That patient is still dead so I cannot have an excuse for reporting my own progress. He was a man, about 60 years of age who was in good health, but about two months before entering the hospital he had jaundice. The jaundice increased. He had two very severe attacks of pain and apparently gallbladder involvement. When he entered the hospital his icteric index was upward to 150. After preliminary treatment I operated upon him expecting to find probably a stone in the end of the common duct though his icteric index was quite high. I found instead the gallbladder thickened and adherent. It was opened and a whitish material was evacuated but in the head of the pancreas was a small infiltrating mass which involved the wall of the duodenum. The duodenum was somewhat contracted so I thought it was probably an early cancer and I excised it. This is the specimen after its removal, showing the duodenum, the common duct, and the pancreatic duct. (Slide) This is the inside of it. (Slide) The adenoma was not cancer. It was fibro-adenoma with considerable infiltration but definitely not cancer.

(Slide) This is the technic that I employed in that case. I had already opened the gallbladder and I had no particular difficulty in excising the duodenum together with a small portion of the infiltrated head of the pancreas. This proved later to be inflammatory and not very extensive, so I brought up this distal end of the duodenum and attached it to the greatly dilated end of the common duct with silk sutures. Then I did the same anteriorly and put in another row of sutures at the pancreatic duct, put in another row of silk sutures and over that sutures of fine catgut, which brought up the duodenum pulled it over the raw surface of the head of the pancreas, and attached it all around to a margin of the pancreatic stomach. In addition, we brought up the fatty tissue omentum and sutured that.

The patient made a very satisfactory operative recovery. He left the table with a pulse of only 88 and in 36 hours he was still doing well. Then he developed symptoms of uremia, passed no urine and died on the fifth day.

At necropsy I found the abdomen was in very good condition. The kidney showed evidence of nephritis. It was hypostatic pneumonia. While the patient died, it looks as though there might be a very limited field for that type of operation in which not much of the pancreas has to be excised.

May I say in connection with these types of operations, the one that Doctor Orr showed and the one of Doctor Brunschwig's in which a loop of duodenum is brought up and attached to the gallbladder that lateral anastomosis between these loops can be made very easily with a little rubber band that I mentioned yesterday. This band can be inserted quickly. It does not open the lumen of the bowel, and it has in no way any originality in the way of elastic ligature which McGraw established years ago. It is merely another application of a principle that he established. Resena for instance, established the principle of using silk and the procedure of Doctor Wangenstein, of course is based on the principle established by Doctor Maddock.

DR LESTER R. DRAGSTEDT (Chicago, Ill.) In 1939 I presented a report before this Association on the significance of lipocais in surgery indicating that a field of usefulness for this substance might appear with the further development of pancreatoduodenectomy in the treatment of cancer of the ampulla and head of the pancreas. At that time there was still some dissent to our conclusion that lipocais is an internal secretion of the pancreas distinct from insulin which is necessary for normal nutrition and life. At present I believe all are agreed that the beneficial effect of the oral administration of whole pancreas or of fat-free alcohol extracts of pancreas in preserving the life of insulin-treated depancreatized dogs and in preventing the usual fatty infiltration of the liver in such

animals cannot be accounted for on the basis of lecithin, choline, betaine, or the general lipotropic action of protein. In a report at the recent meeting of the American Physiological Society we have also presented evidence indicating that inositol is not the active principle of lipocaic. There seems no reason to doubt that lipocaic is a specific substance, probably protein in nature, manufactured by and present in the pancreas, which is necessary for life and for the normal transport and utilization of fat.

While adequate data are not yet available, it seems likely that following complete pancreatectomy in man both insulin and lipocaic will be required. The situation resulting from excision of the head of the pancreas and adjacent duodenum is more obscure. In this case pancreatic juice fails to reach the duodenum and more or less extensive degeneration of the pancreas results from the occlusion of the ducts. The absence of pancreatic juice may be expected to produce some impairment in the digestion and absorption of fat. Doctor Vermeulen, in our laboratory, has recently found that the depancreatized dog absorbs only 70 per cent of the food fat, whereas in the normal animal absorption is practically complete. This defect in digestion and absorption of fat is not corrected by lipocaic and is little influenced by the administration of pancreatin or pancreatic juice. It should be emphasized that there is at present no evidence that lipocaic affects the digestion or absorption of fat under any conditions. The development of fatty infiltration of the liver and the other sequelae of lipocaic deficiency following occlusion of the pancreatic ducts in the dog depends apparently on the extent of pancreatic degeneration that follows this procedure. Of 19 animals in our laboratory, in which this operation was done, only four developed fatty livers. Doctor Brunschwig excised the head of the pancreas and ligated the ducts in two monkeys. Neither of these developed a fatty liver. I recently excised the head of the pancreas and adjacent duodenum in a man for carcinoma of the ampulla and common bile duct. This man survived for four months, and at death the liver contained no excess fat although the pancreatic ducts were found to be obstructed, markedly dilated, and the pancreas degenerated. However, until a good deal more data on man become available it would seem wise to watch these patients carefully for evidence of developing lipocaic deficiency. This may be manifested by progressive loss of weight and strength, hepatomegalia and impaired liver function as revealed by the bromsulfalein excretion and hippuric acid synthesis tests. Profound alterations in the concentration of blood lipids may be found. In dogs with lipocaic deficiency, the blood lipids are usually reduced to approximately one-half the normal values. In man, however, we have seen a number of cases of hypercholesterolemia, hyperlipemia, hepatomegalia, and xanthomatosis, where the administration of lipocaic has brought about a dramatic chemical improvement and return of the abnormal blood chemistry toward normal levels. Lipocaic deficiency in man may, therefore, in some instances be indicated by increase rather than decrease in the lipid constituent of the blood.

DR VERNE C HUNT (Los Angeles, Calif.) Since reporting before this Association, a year ago, four cases of ampullary carcinoma that we had operated upon successfully, I have had occasion to operate upon another similar case, in which I performed a modification of the so-called Whipple radical operation, which makes a total of five cases of ampullary carcinoma that we have successfully operated upon without surgical mortality.

The first two of these, as some of you will recall, were by transduodenal excision, and the last three by resection of the duodenum and the head of the pancreas. These were done as one-stage, if one is willing to accept as one-stage operation the procedure of the resection of the duodenum, duodenectomy, and resection of the head of the pancreas.

All of these five cases occurred in our private surgical practice. I speak of that for two reasons. First of all, it is indicative to me that this lesion is not as uncommon as we are led to believe, when there are that number of cases in a small private surgical practice. I speak of this also because of the fact that these five patients were subjected to an early surgical viewpoint, in contradistinction to what I believe is true in many Services, particularly in Medical Services, where many of these patients come in and are placed on the medical wards, where they are subjected to prolonged and repeated differential diagnostic séances, so to speak. The point I want to make is that there is just one way to make diagnosis of this lesion, and that is on surgical exploration.

I have about taken the position that no patient with obstructive jaundice should be allowed to die without surgical aid. I mean that both ways. There are some patients

who may die following surgical exploration. However I would much rather have them die following a surgical exploration for an inoperable lesion than die a medical death with no opportunity for surgical exploration. There are few internists and medical men who are aware of the fact that surgery has possibilities in this area.

(Slide) This patient was operated upon last October in whom we performed a one-stage resection total duodenectomy and resection of the head of the pancreas.

(Slide) We performed the operation of resection of the head of the pancreas at the open end of the duodenum. This shows a slide of the pancreas removed and I think you see the well demarcated scar.

(Slide) You will be interested in the results of these patients. This is Case 4 that I reported a year ago. I bring it back to you again to refresh your memory and show you there is retroperitoneal lymph node involvement. This patient is living and clinically well 13 months following operation. I might say that of the five patients we have operated upon four of them are living. The first one with transduodenal resection that I reported a year ago is living nearly three years with retroperitoneal metastasis no longer present. At least the patient is subjectively well and we have no grounds to-day to believe that the patient has metastasis. We have another one living following the radical operation of two years and one month and this one one year and one month and the last case seven months.

(Slide) I wish to show this slide for two reasons. Whatever the facts may be regarding the value of preserving pancreatic secretion (external pancreatic secretion) I was very much interested in what Doctor Dragstedt had to say. As you all probably know who are interested in this field of surgery the observations and conclusions of Doctor Dragstedt and of Doctor Montgomery in San Francisco are quite at variance regarding the effect of the external secretion of the pancreas on lipid metabolism. Whatever subsequent events may prove to be the fact I believe it is still paramount whenever it is possible to preserve pancreatic secretion and I think in many instances it can be done.

DR HERMAN E PEARSE JR (Rochester N Y) Doctor Whipple has mentioned that I suggested the use of the end of the jejunum to anastomose to the biliary tract. I did this because I excised all the duodenum.

I wish to say one word about this. As the scope of the operation is enlarged to remove all of the head and the uncinate process of the pancreas one may interfere with the circulation of the distal duodenum. Recently I lost a case because I did not include the duodenum when I made such an excision. The patient died and at necropsy the stump of the duodenum that I had allowed to remain had become necrotic and peritonitis developed from the breakdown of the suture.

DR ASHLEY W OUGHTERSON (closing) There was so much interest expressed in this subject and the subject was so well covered that I have little more to add.

In the first place I would like to say that there are many studies which I did not have time to go into in relation to liver function fats etc., but several of our patients did have a very markedly diminished liver function which seemed at least to warrant a two-stage procedure in order to give additional safety. And I must say Doctor Harvey is rather on the other side.

In regard to the indispensability of the external secretion perhaps nine months of the year is a short time to regard that as being finally solved but certainly for that period some of these patients at least get along on a normal diet without any difficulty.

In regard to typical fatty stools and the use of pancreatin and lipocalc on the one patient it had no influence.

It is also worthy of note that this is the only patient who had a severe avitaminosis preceding the operation and the same avitaminosis afterward which so far they have been unable to correct.

POSTOPERATIVE NITROGEN LOSS AND STUDIES ON PARENTERAL NITROGEN NUTRITION BY MEANS OF CASEIN DIGEST*

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THE NITROGEN METABOLISM of the surgical patient has been the subject of special consideration in recent years. The possibility of parenteral administration of nitrogenous foodstuff further extends the practical aspects of this problem.

A major surgical procedure with operative manipulation of deeply situated viscera and tissues followed by a brief period of starvation and then gradual return, over several days, to ingestion of normal diet constitutes together with the complications often developing, such as shock, fever, vomiting, the presence of injured tissues, *etc*, an altered physiologic state. Because intake of nitrogen obviously does not equal output during this period a state of negative nitrogen balance exists for varying periods. Operative trauma itself may be the cause of increased nitrogen catabolism (so-called toxic (?) destruction of protein).

In order to obtain some concrete conception of the extent of this loss, in 41 patients subjected to major operations of various types, nitrogen balance studies were carried out from the day of operation to and including the tenth postoperative day.

Urine, feces, excess sputum, biliary or other drainage, vomitus and gastric aspirations were collected each 24-hour period and analyzed for nitrogen (Micro-Kjeldahl), and this was compared with the nitrogen intake each day. The latter was obtained from standard dietitians' charts and this portion of the data represents, therefore, an approximation, since it was not practical to analyze each sample of food received from day to day for the exact nitrogen content.

The conditions pertaining to the postoperative management in this group of patients were (a) Where the abdomen or thorax was not opened liquids were permitted by mouth as soon as tolerated and shortly thereafter a soft or regular diet was given, the latter being taken by the third to fifth postoperative day, and (b) where the abdomen or thorax was opened nothing was taken by mouth for the first 48 to 72 hours, fluids being given parenterally, on the third or fourth day small quantities of water were taken at hourly intervals, the next day clear liquids, and if tolerated soft to regular diet ingested by the sixth or seventh day, except in operations upon the stomach, where increase in food by mouth was more gradual.

* This work was conducted under a grant from the Mead-Johnson and Company, Evansville, Ind.

* Read before the American Surgical Association, Cleveland, Ohio April 6-8, 1942

Blood transfusions which were given in many cases following operation have not been taken into account in calculating the nitrogen balance

The results of the studies on net nitrogen loss (or gain) over the ten-day postoperative period are shown in Table I

TABLE I
NET LOSS OR GAIN IN NITROGEN IN TEN DAY POSTOPERATIVE PERIOD IN 41 PATIENTS
UNDERGOING A VARIETY OF MAJOR SURGICAL PROCEDURES

Operation	Patient	Net N Loss or Gain 10 day P O period
Thoracic sympathectomy	L M	- 27 10 Gm
	McM	- 68 47 Gm
Esophagoplasty	Ril	- 75 17 Gm
Exploratory celiotomy	Windb	- 65 37 Gm
	Bernst	- 16 86 Gm
	Valent	- 3 81 Gm
Acute append (peritonitis)	Ad	- 49 17 Gm
Gastric resection	Neh	- 73 53 Gm
	Maz	-175 79 Gm
Repair perforated peptic ulcer	Ly	-136 06 Gm
Cholecystectomy	Fish	- 24 34 Gm
	Thomp	- 27 78 Gm
	Miller	- 23 18 Gm
	Lew	- 20 74 Gm
	Barger	- 75 90 Gm
	Patton	- 24 73 Gm
	Bohl	- 68 65 Gm
	Glynn	+ 5 91 Gm
	Clayt	- 36 44 Gm
	Mal	+ 1 13 Gm
	Pears	-114 09 Gm
Radical mastectomy	Rawl	+ 1 23 Gm
	Meed	- 15 68 Gm
	Shaw	- 13 51 Gm
Operation on extremities	Burdi	- 9 98 Gm
	Kit	- 6 21 Gm
	Gal	- 30 00 Gm
Thyroidectomy	Anth	+ 4 44 Gm
Herniotomy	Berb	- 18 35 Gm
Gastro enterost	Hag	- 47 96 Gm
Partial colectomies	Robert	- 20 72 Gm
	Boyer	- 60 22 Gm
	Zaraz	- 51 86 Gm
	Benk	- 49 48 Gm
	Schr	- 69 87 Gm
	Ehl	+ 4 97 Gm
	Steph	- 41 44 Gm
	Thomp	- 59 88 Gm
Operations on pancreas	Rapacz	- 39 96 Gm
	Fait	- 24 41 Gm
	Cullen	- 61 02 Gm

NITROGEN LOSS

TABLE I A

SUMMARY OF DATA IN TABLE I ON NITROGEN LOSS IN TEN-DAY POSTOPERATIVE PERIOD

- (A) Group I 18 patients lost up to 40 Gm of nitrogen, average = 21.31 Gm
 Group II 7 patients lost 41 to 60 Gm of nitrogen average = 51.4 Gm
 Group III 11 patients lost 61 to 175.8 Gm nitrogen, average = 89.45 Gm
 Group IV 5 patients gained 1.13 to 5.91 Gm nitrogen, average = 3.54 Gm
 (B) Calculated *dry weight of protein lost (Group I) = 133.19 Gm, this represents †0.67 Kg wet body tissue
 Calculated *dry weight of protein lost (Group II) = 321.25 Gm, this represents †1.6 Kg wet body tissue
 Calculated *dry weight of protein lost (Group III) = 549 Gm, this represents †2.7 Kg wet body tissue
 * Grams of excreted nitrogen $\times 6.25$
 † Calculated on assumption that the relationship of tissue protein to water in the tissues is 1:5 (Best and Taylor Physiological Basis of Medical Practice 2nd ed Baltimore Williams Wilkins, pp 915-916, 1940)

There seemed to be no correlation between age, sex, type of anesthesia, the presence or absence of malignant neoplasm or other type of disease, and the extent of nitrogen loss. The most important factor in this connection appeared to be the period of postoperative starvation and period of limited intake of food. Moderate brief rises in temperature did not affect nitrogen excretion to a very marked degree. Indeed, the patient in whom the postoperative nitrogen loss was greatest (175.79 Gm) had had a Pólya-type partial gastrectomy and for the ten-day period was afebrile but ate practically no food because of intractable vomiting, recovery eventually ensued. Where the individual could tolerate food relatively early and ingested a relatively liberal diet there was a small net loss or even a positive nitrogen balance at the end of the ten-day period. A study of the day-to-day nitrogen balance revealed that the major portion of the net loss occurred during the first five days postoperatively when food by mouth was not permitted or was very limited.

The practical importance of an effective method for parenteral administration of nitrogenous foodstuff in postoperative management where intake by mouth would of necessity be limited, especially for prolonged periods and in debilitated persons, is obvious. This would reduce or even prevent significant loss of nitrogen. Such a possibility would appear to be afforded by the intravenous injections of casein digest which Elman in 1937, and reporting before this Association in 1940, demonstrated for the first time to be feasible in man. Our own studies were concerned with obtaining pertinent data on the question of the clinical use of casein digests.

The casein digest (Amigen) employed by us in the observations recorded below was kindly furnished by Mead-Johnson and Company, Evansville, Ind., and represents an enzymic hydrolysate of casein (complete protein). Mueller, Kemmerer, Cox, and Barnes found that young rats on a diet, the nitrogenous portions of which consisted of the digest, grew and developed normally, and that dogs with hypoproteinemia regenerated plasma proteins with the digest given by mouth as the sole source of nitrogen. Clark, Brunschwig, and Corbin showed, for the first time, that dogs depleted of protein stores and exhibiting hypoproteinemia as a result of several weeks on a synthetic *nitrogen-free* diet regenerated plasma proteins when this diet was continued and supplemented by daily intravenous injections of the digest as the sole source of nitrogen. These experiments are summarized in Table II.

TABLE II

(Reproduced from Proc Soc Exp Biol and Med 49 282-285 1942)

SUMMARY OF EXPERIMENTS ON PLASMA PROTEIN REGENERATION WITH INTRAVENOUS INJECTION OF CASEIN DIGEST (AMICEN)

Dog	Depletion period N free diet days	Duration of inj days	Avg daily casein digest intrav (10% sol) c c	Beginning	End
				of inj period	
Eddie Exp I	47	12	165	Wt Kg	6 7 6 1
				Total P P * Gm %	4 06 5 64
				Hematocrit	39 34 2
				R B C † M	6 2 5 8
Eddie Exp II	21	17	177	Wt Kg	7 0 6 2
				Total P P Gm %	4 66 4 91
				Hematocrit	41 32
				R B C M	8 5 8
Fuzzy Exp I	27	21	248	Wt Kg	9 2 8 3
				Total P P Gm %	4 74 5 12
				Hematocrit	43 35
				R B C M	7 5 0
Fuzzy Exp II	37	15	210	Wt Kg	9 1 9 2
				Total P P Gm %	4 31 4 97
				Hematocrit	43 35
				R B C M	6 1 6 0
Pete	77	18	309	Wt Kg	7 4 6 6
				Total P P Gm %	5 0 5 97
				Hematocrit	37 25
				R B C M	7 5 4 7
Mike	21	11	256	Wt Kg	8 6 8 1
				Total P P Gm %	3 98 4 99
				Hematocrit	38 2 27
				R B C M	7 5 6 14
Kate	76	7	214	Wt Kg	8 1 7 6
				Total P P Gm %	5 31 5 7
				Hematocrit	40 36
				R B C M	5 5 6 1

* Plasma protein

† Red blood count

The manner of injection of casein digest varied with the individual patient, the total amount of fluid to be administered, and the sensitivity of the patient to the injections. The product was received, sterile, in bottles containing approximately 1,000 cc of a 10 per cent aqueous solution of the digest, thus representing 100 Gm of hydrolyzed casein or approximately 12 Gm of nitrogen. In these studies it was administered in one of the following forms:

- (1) Intravenously as a 10 per cent solution (hypertonic)
- (2) Intravenously with equal parts of 5 per cent or 10 per cent dextrose in distilled water (hypertonic)
- (3) Intravenously with two parts of distilled water (isotonic)
- (4) By hypoclisis, one part casein digest, two parts of distilled water (isotonic)
- (5) Intravenously as 10 per cent solution with equal parts of normal saline or Ringer's solution

Further data concerning the casein digest is as follows

One hundred Gm of digest yields approximately 12 Gm nitrogen. One gram of digest is approximately equivalent to 3.66 calories. Studies on guinea-pigs, carried out by H. C. Hopps and J. Campbell, of the Department of Pathology, confirmed the fact that the product was not anaphylactogenic.

Additional quantities of saline or Ringer's solution may be administered to afford adequate electrolyte. Where 50 Gm of protein were desired as supplementary nourishment, 500 cc of the 10 per cent solution were mixed with a liter of triple distilled water and injected either by hypodermoclysis or intravenously.

Nitrogen equilibrium can ordinarily not be achieved on a pure protein diet, thus simple injection of a quantity of digest equivalent to the standard protein requirement of a given individual will obviously not suffice to prevent nitrogen loss. Caloric requirements must be met to a substantial degree by carbohydrate (and fat) which afford energy and thus spare, so to speak, the amino-acids for protein synthesis, otherwise the amino-acids themselves will be catabolized for sources of energy. Thus, where nourishment is given entirely by the intravenous route the casein digest must be combined with glucose.

TABLE III

NITROGEN BALANCE STUDIES SHOWING FAILURE TO ACHIEVE NITROGEN EQUILIBRIUM IN PATIENTS RECEIVING QUANTITIES OF PROTEIN (CASEIN DIGEST) AND INADEQUATE GLUCOSE DURING PERIODS OF OBSERVATION

Days	Patient J. O. †				Patient Schoendt ‡				Patient Whit ‡			
	Gm N Excr	Gm N Inj	Gm N Bal	Gm Dext Inj	Gm N Excr	Gm N Inj	Gm N Bal	Gm Dext Inj	Gm N Excr	Gm N Inj	Gm N Bal	Gm Dext Inj
1	8.91	0.00	-8.91		12	5.80	+6.20	70	4.09		4.09	
2	6.0	9.19	-3.19	75	19.15	12.00	-7.15	150	10.09	6.00	-3.91	75
3	26.7	12.00	-14.70	150	22.00	12.00	-10.00	150	12.18	6.00	-6.18	75
4	25.30	12.00	-13.30	150	21.33	12.40	-9.33	150	14.74	6.00	-8.74	75
5	26.70	12.00	-14.70	150	14.41	12.00	-2.41	75	14.37	6.00	-8.37	75
6	22.60	12.00	-10.60	150	18.60	12.00	-6.60	150	10.39	6.00	-4.39	75
7	20.09	0	-20.09	150	17.51	12.00	-5.51	150	12.15	6.00	-6.15	75
8	20.95	18.00	-2.95	75	17.65	12.00	-5.65	150	12.55	6.00	-6.55	75
9	23.30	18.00	-5.30	75	20.75	12.00	-8.75	150	9.00	6.00	-3.00	75
10	20.10	18.00	-2.10	75	18.59	12.00	-6.59	150	15.02	12.00	-3.02	75
11	21.60	18.00	-3.60	75	11.80	12.00	+0.20	150	13.33	12.00	-1.33	75
12	20.03	18.00	-2.03	75	16.50	12.00	-4.50	150	16.95	12.00	-4.95	75
13	23.30	18.00	-5.30	75	7.75	12.00	+4.23	150	14.12	12.00	-2.12	75
14	24.60	18.00	-6.60	75	16.00	12.00	-4.00	150	15.14	12.00	-3.14	75
15	22.9	18.00	-4.90	75	14.04	12.00	-2.04	150	13.91	12.00	-1.91	75
16	27.30	18.00	-9.30	75	19.77	12.00	-7.77	150	16.17	12.00	-4.17	75
17	17.31	12.00	-5.31	75	18.53	12.00	-6.53	150	12.74	12.00	-0.74	75
18	13.94	12.00	-1.94	75	17.63	12.00	-5.63	150	10.98	12.00	+1.02	75
19	15.92	12.00	-3.92	50	22.3	18.00	-4.30	100	7.61	12.00	+4.39	75
20	17.18	9.00	-8.18	75	18.49	18.00	-0.49	100	12.30	12.00	-0.30	150
21	14.39	18.00	+3.61	75	22.50	8.00	-14.50	100	13.11	12.00	-1.11	75
22	21.30	18.00	-3.30	75	11.64	8.00	-3.64	100	13.23	12.00	-1.23	150
23	13.45	9.00	-4.45	150	22.80	8.00	-14.80	100	9.72	12.00	+2.28	150
24					Total N loss = 119.56 Gm				17.92	12.00	5.92	63
25	16.75	18.00	+1.25	75					14.12	12.00	-2.12	63
26	14.74	18.00	+3.26	75					Total N loss = 70.88 Gm			
27	20.70	18.00	-2.70	75								
Total N loss = 140.05 Gm												

* J. O. M. age 23 (274746), regional ileitis, partial enterectomy, wt 66 Kg.

† Schoendt M. age 36 (87546), regional ileitis, partial enterectomy, wt 81 Kg.

‡ Whit M. age 57 (277337), Ca stomach, total gastrectomy, wt 61.5 Kg.

The details of the nitrogen balance in three patients receiving nothing by mouth and glucose and amino-acids in the form of casein digests over rather prolonged periods are summarized in Table III and the failure to obtain nitrogen equilibrium is well demonstrated since, while the caloric requirements were nearly satisfied, there was obviously insufficient quantity of carbohydrate to spare amino-acids. On the other hand, in patients J O and Whit some of the daily losses of nitrogen were small enough to warrant the assumption that nitrogen loss was to some extent spared by the quantity of glucose injected.

It would appear that there are individual variations in metabolism and that in the exceptional instance postoperative nitrogen loss may be consistently and appreciably reduced and nitrogen equilibrium achieved with parenteral carbohydrate and casein digest, even where the proportions of

TABLE IV

NITROGEN BALANCE STUDY OF PATIENT RECEIVING NOTHING BY MOUTH AND CASEIN DIGEST AND GLUCOSE INTRAVENOUSLY SHOWING SPARING EFFECT OF DIGEST ON NITROGEN LOSS

Mrs Rasg (274120) F age 36 Ca stomach resection wt 50 Kg

Days	Gm N Inject	Gm N Excret	Gm N Bal	Gm Dext Inject
1	0	2 46	2 46	50
2	0	2 71	- 2 71	125
3	0	9 28	- 9 28	25
4	0	19 43	-19 43	100
5	6 00	- 9 10	- 3 10	75
6	12 00	-17 13	- 5 13	75
7	12 00	-14 64	- 2 64	100
8	12 00	-12 75	75	75
9	6 00	-13 27	- 7 27	75
10	12 00	-11 99	+ 01	50
11	12 00	-12 79	- 79	75
12	15 60	-12 81	+ 2 79	75
13	18 00	-18 84	- 84	75
14	18 00	-18 66	- 66	75
15	18 00	-18 27	- 27	75
16	18 00	-22 72	- 4 72	75
17	18 00	19 37	- 1 37	75

Total loss N during 12 day period of injection of casein digest = 24 80 Gm

these two foodstuffs are not ideal. The nitrogen balance studies in such a case are summarized in Table IV. During the 13 days in which the casein digest together with glucose was administered, nitrogen equilibrium was almost achieved in five days, was achieved on one day and on one day a positive nitrogen balance obtained. The total loss of nitrogen during the 12-day period in which casein digest and carbohydrate were injected was 24 80 Gm, which is no greater than in a number of patients subjected to the routine postoperative management in regard to permission for ingestion of food as soon as possible.

Where there has been depletion of nitrogen stores because of prolonged vomiting and consequent reduced intake, casein digests and carbohydrate in proper amounts and relative proportions might facilitate replenishment of the stores where this would take a longer period by ingestion of food alone, especially where the appetite is poor.

NITROGEN LOSS

TABLE V

SHOWING POSITIVE N BALANCE IN PATIENT (WITH TERMINAL STAGE OF CARCINOMA) AFFORDED BY INTRAVENOUS INJECTION OF CASEIN DIGEST SUPPLEMENTING LOW PROTEIN DIET

Pt Lak, M age 50 (270426), wt 60.3 Kg, inop, Ca pancreas, prev cholecystogastrostomy

Observation Days	Intrav N Gm	N by Mouth Gm	N Excr Gm	N Bal Gm	Dext (per os) Gm	Fat (per os) Gm
1		6.60	7.29	- 6.9	252	87
2		6.30	8.65	- 2.35	316	94
3		2.70	3.80	- 1.10	178	74
4	18	0	10.62	+ 7.38	0	0
5	18.00	75	7.86	+ 10.89	100	18
6	18.00	75	14.37	+ 4.38	112	26
7	14.00	90	7.86	+ 7.04	100	32
8	12.00	1.95	13.52	+ 43	135	42
9	12.00	1.65	5.32	+ 8.33	116	50
10	12.00	1.50	7.56	+ 5.94	140	43
11	12.00	3.00	12.86	+ 2.14	160	78
12	12.00	1.20	13.65	- 45	105	35
13	12.00	1.75	9.74	+ 3.01	142	46
14	12.00	2.10	10.76	+ 3.24	162	53
15	12.00	1.95	4.85	+ 9.10	130	53
16	12.00	1.95	12.77	+ 1.18	139	53
17	12.00	1.20	14.68	- 1.48	122	34
18	12.00	1.20	15.48	- 2.28	157	30
19	6.00	1.00	5.35	+ 1.65	112	16

Net positive N balance in 16 day period = 127.94 Gm (Calculated equivalent to 4 Kg of protein with water in the body)

An example of this is afforded by the nitrogen balance studies of the patient summarized in Table V. He presented advanced carcinoma of the head of the pancreas, had had a cholecystogastrostomy some weeks previously and was brought back to the hospital because of increasing weakness and a recent severe gastro-intestinal hemorrhage. As shown in the table, the nitrogen balance was negative during a three-day period when choice of food was left to the patient. Beginning with the fourth day, a low protein diet was prescribed and casein digest injected intravenously each day. The plasma proteins were low (5.5 Gm per cent) indicating a depletion of protein stores. On the combination of intravenous digest and diet by mouth, the patient was put into positive N balance and at the end of the sixteenth day of the injection period, presented a net gain in nitrogen of 127.94 Gm which is equivalent to 800 Gm of protein dry weight and 4,000 Gm of protein with water as body weight (or 88 lb). Clinically, the patient did not make progress, continued to complain of loss of appetite and on the day following the last recorded studies died suddenly of massive hemorrhage into the bowel. Necropsy revealed abdominal carcinomatosis, and the source of the hemorrhage was neoplasm fungating into the duodenum from the head of the pancreas. However, these studies illustrate the possibility of forced nitrogen nutrition by the intravenous route and the avidity for nitrogen of an organism depleted of nitrogen, although there obtained a fatal disease process which was in the terminal stages.

In another series of observations, patients not suffering from a fatal condition and who were subjected to a major surgical procedure received casein digests postoperatively beginning with the day of operation and later in

supplement to the usual postoperative dietary regimen. The purpose of these studies was to obtain data on the extent of sparing excess protein catabolism. The nitrogen balance studies are summarized in Table VI, and show that in

TABLE VI

SUMMARY OF POSTOPERATIVE NITROGEN BALANCE STUDIES IN THREE PATIENTS SUBJECTED TO MAJOR SURGICAL PROCEDURES AND RECEIVING CASEIN DIGESTS AND GLUCOSE INTRAVENOUSLY FROM THE DAY OF OPERATION AND IN SUPPLEMENT TO USUAL POSTOPERATIVE DIETARY MANAGEMENT

Patient I Mrs T cholecystectomy wt 62.9 Kg

Days	1	2	3	4	5	6	7	8	9	10
N Intrav Gm	6.00	18.00	18.00	18.00	0	9.6	0	0	0	0
N Mouth Gm	0	0	0	0	1.40	4.64	5.10	2.1	3.0	4.60
N Excret Gm	-4.54	16.29	21.5	17.85	8.12	9.94	4.52	3.04	7.55	4.24
N Bal Gm	+1.46	+1.71	-3.50	+1.15	-6.72	+3.30	+5.8	-9.4	-4.55	+3.6
Dext Gm	75	75	90	105	80	81	79	65	115	107
Fat (per os) Gm					10	47	48	21	40	43

Net N loss 10 day period = -8.5 Gm

Patient II Mr L cholecystectomy wt 80.5 Kg

N Intrav Gm	18	18	18	18	18	18	18	18	18	0
N Mouth Gm						0.45	6.70	6.70	9.6	12.6
N Excret Gm	13.71	23.3	28.4	23.17	20.79	17.69	17.60	14.3	10.05	8.1
N Bal Gm	+4.29	-4.70	-10.4	-5.17	-2.79	+7.6	+7.10	+10.40	+17.10	+4.50
Dext Gm					160	24	160	213	260	337
Fat (per os) Gm						98	107	82	140	152

Net N gain 10 day period = 20.39 Gm

Patient III Mrs S cholecystectomy wt 76.6 Kg

N Intrav Gm	6.00	6.00	12.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
N Mouth Gm	0	0	0	0	0	4.00	6.40	8.00	11.10	13.25
N Excret Gm	3.32	7.54	16.57	13.26	12.00	7.16	8.59	11.36	10.98	12.00
N Bal Gm	+2.68	-1.54	-4.57	-7.26	-6.00	+2.84	+3.81	+3.64	+4.12	+7.25
Dext Gm	150	150	300	161	175	120	161	205	190	249
Fat (per os) Gm				4	0	33	78	75	101	108

Net N gain 10 day period = 4.97 Gm

one case the net loss of nitrogen was only 8.5 Gm, in one there was a net gain of 20.39 Gm and in the third a net gain of 4.97 Gm. These were not selected cases and indeed did not present entirely smooth immediate postoperative courses. Patient I also suffered from severe menopausal symptoms and complained of severe nausea with frequent vomiting during the first four days (not due to ileus or postoperative dilatation of the stomach). Patient II was a chronic alcoholic and developed temperatures of 102° F on the second and third days. Patient III was very apprehensive following the operation and resented all parenteral fluids. The casein digest was given to this patient by hypodermoclysis on all but the third day.

The vast majority of patients subjected to major surgical procedures recover without special attention to nitrogen balance, since the brief period of total and relative nitrogen starvation is well tolerated by the organism and the loss is made good after return to full diet. However, following major surgical operations there is frequently a rather prolonged asthenia which is often appreciable for a few weeks after discharge from the hospital. Leriche has referred to this syndrome, which cannot be clearly defined as "maladie postopératoire," and ascribed it to generalized disturbances of the sympathetic nervous system. It is interesting to speculate on the possible rôle of postoperative nitrogen loss in this connection. While the quantity of tissue pro-

tein lost may not be large, the source of the catabolized protein under these conditions is not known and might conceivably differ from the stores depleted, when in the course of usual activities the subject may simply refrain from protein foods and continue his activities. Patient II in Table VI in whom there was a net gain of 20.39 Gm. commented upon the fact that he felt quite well at this time and did not experience the weakness which he had expected to occur for some days following the operation. His weight a day before operation was 80.5 Kg. and on discharge on the sixteenth day was 80 Kg., a net loss of 0.5 Kg. or 1.1 pounds. It would be difficult indeed to evaluate the benefits in any large series of patients derived from substantial sparing or actual prevention of postoperative nitrogen loss, but it is understandable theoretically that in such a group the period of impaired physical activity due to postoperative asthenia might be shortened.

Minimal caloric requirements including sufficient protein (as amino-acids) may be met by intravenous nutrition and in this way facilitate operative procedures and contribute to recovery. The nitrogen balance studies shown in Table VII are of a white female patient, age 36, in whom a large fungating

TABLE VII

SUMMARY OF NITROGEN BALANCE STUDIES IN PATIENT WITH OBSTRUCTION IN SIGMOID DUE TO INFLAMMATORY MASS IN PELVIS

Mrs. R. F. age 36 (276536) wt. 50 Kg. Left tubo-ovarian abscess with adhesions to sigmoid colon producing obstruction

Days	N Inj Gm	N by Mouth Gm	N Exc Gm	N Bal Gm	Carbohydrate Gm	Fat Gm
1	18.00	0	4.98	+13.02	300	
2	18.00	0	10.32	+7.68	300	
3	18.00	0	10.60	+7.40	300	
4	18.00	0	12.39	+5.61	300	
5	18.00	0	15.16	+2.84	300	
6	18.00	0	14.10	+3.90	300	
7	18.00	0	17.45	+55	300	
8	18.00	0	15.58	+2.42	300	
9	18.00	0	13.80	+4.20	300	
10	18.00	0	14.78	+3.22	300	
11	6.00	0	8.59	-2.59	300	
12	6.00	0	7.03	-1.03	150	
13	6.00	0	5.09	+91	0	
14	12.00	0	12.68	-68	150	
15	12.00	0	16.92	-4.92	150	
16	18.00	0	13.00	+5.00	300	
17	8.4	0	14.12	-5.72	150	
18	0	1.00	8.04	-7.0	53	15
19	0	1.98	4.41	-2.43	99	30
20	6.00	7.00	9.15	-1.17	126	18
21	6.00	7.2	7.57	+5.43	184	98
22	6.00	6.04	7.29	+4.75	211	93
23	6.00	6.10	5.44	+6.66	158	83
24	6.00		8.96			

mass was excised from the cervix on the gynecologic service. Because of the histologic diagnosis of leiomyosarcoma external radiation was given. A left adnexal mass was also palpated and regarded as an extension of the tumor with inflammation. Frequent nausea and vomiting occurred at home for a number of days after discharge from the hospital. She was readmitted and

the symptoms continued for some ten days, the patient retaining almost nothing by mouth but receiving fluids parenterally. When one of us (A. B.) was requested to see the patient because of the question of low colon obstruction, there was moderate distention of the abdomen and rectal examination revealed what appeared to be constricting bogginess about the rectal colon. Barium enema revealed a high degree of obstruction over several centimeters of a redundant segment of the lower sigmoid in the pelvis. The stomach was aspirated and a small quantity of liquid recovered. Nothing was then permitted by mouth. Intravenous nutrition was carried out daily by means of the following solutions:

- (A) 1 500 cc 10 per cent casein digest } mixed in the flask
 1 500 cc 10 per cent dextrose }
 (B) 1 500 cc 10 per cent dextrose in normal saline

After solution A was injected, solution B was poured into the flask. The total period of injection lasted five to six hours, the total daily fluid intake was 4,500 cc. The patient soon learned at what rate nausea and other disagreeable sensations could be avoided and the clamp on the tube from the flask was placed within her reach so that she regulated the speed of intake herself.

The caloric content of the above solution is

$$\begin{array}{rcl} 150 \text{ Gm casein digest} \times 3.66 & = & 549 \text{ calories} \\ 300 \text{ Gm dextrose} \times 4.00 & = & 1200 \text{ calories} \\ \hline & & 1749 \text{ calories} \\ \text{NaCl content} & = & 13.5 \text{ Gm} \end{array}$$

Since the patient weighed approximately 50 Kg, the caloric content equaled 35 calories per Kg, and the protein content equaled 3 Gm per Kg. The salt content is slightly in excess of the quantity (10 to 12 Gm) usually ingested by adults on a general diet. Thus basal dietary requirements in energy and protein seem to have been satisfied, although of course vitamins and complete variety of minerals were not provided since it was not anticipated that complete parenteral nutrition was to be maintained for an unusually prolonged period. This factor, however, may easily be adjusted. The nitrogen balance studies show a positive balance over the ten-day period when 18 Gm of nitrogen were injected (1,500 cc 10 per cent casein digest) each day, on the eleventh and twelfth days of observation the latter injections were reduced to 500 cc per day. Clinically, the patient improved markedly on parenteral nutrition. Nausea and vomiting soon ceased, distention disappeared, and gas was passed per rectum. A second barium enema taken on the eleventh day of the injection period showed disappearance of the obstruction in the lower sigmoid except for one point of partial constriction. An exploratory celiotomy was performed on the thirteenth day of the study and the left lower quadrant mass found to be a tubo-ovarian inflammatory process. This was removed dissecting about 15 cm of adherent sigmoid colon from it. As seen in Table VII, a slight positive nitrogen balance was maintained on the day of operation and a slight negative balance obtained on the following day. Due

to the long period of intravenous injections, even prior to the use of casein digests, the superficial veins were rendered unfit for further intravenous therapy by the fifth day after operation. Furthermore, in view of the removal of the obstruction in the lower sigmoid, a soft diet was permitted by mouth and 1,500 cc of 3.5 per cent casein digest injected subcutaneously as supplementary nourishment on the eighth to twelfth postoperative days. A review of the data shows that during the course of this study a positive nitrogen balance was maintained with caloric requirements throughout the 12 days prior to operation, the patient receiving nothing by mouth. A net gain in nitrogen amounting to 47.22 Gm was observed in this period. For the 12 days postoperative, there was a daily variation in nitrogen balance, food was permitted on the sixth day and supplemented by continued parenteral nitrogenous nutrition. At the end of the twelfth day, the net nitrogen gain was 0.63 Gm for the postoperative period, practically, nitrogen equilibrium was maintained. For the whole 24-day period during which food was taken by mouth only for the last five days, caloric requirements were for the most part met and the net nitrogen gain was 47.85 Gm.

Untoward Reactions—While the administration of the casein digest was not in our experience with hundreds of individual injections accompanied by serious reactions (with exceptions to be noted below), minor disturbances were frequent. These include mild and occasionally severe nausea, and vomiting and a generalized disagreeable flushing sensation. In the exceptional instances, these are sufficiently pronounced to warrant discontinuation of injections after one or several attempts. On the other hand, we have observed nausea and a generalized feeling of discomfort to be present during the first few injections and to disappear subsequently as they are continued. In one patient marked nausea developed with the first injections but after several days she was observed to eat simultaneously while receiving the digest intravenously. An important factor is the speed of injection. This should be altered with each patient. Some individuals exhibited no discomfort from 500 cc of the 10 per cent aqueous solution administered in 30 to 45 minutes. Where intravenous injections are not well tolerated, a 3.3 per cent solution in distilled water may be given safely by hypodermoclysis without discomfort and without reaction in the tissues. Another feature frequently encountered, is reduction in desire for food apart from any nausea or other discomfort. Patients with clinical icterus are not suitable subjects for intravenous injections of the casein digest, since in three instances severe chill, marked rise in temperature, and profound discomfort resulted from the initial injection. In another instance, a chronic alcoholic with marked liver damage, as shown by the hippuric acid liver function test, a similar reaction accompanied the initial intravenous injection but hypodermoclyses of the 3.3 per cent solution were well tolerated for several days. On the other hand, patients who had been icteric and the latter condition cleared, did tolerate intravenous administration of the digest. It would appear that in certain types of acute hepatitis a sudden flooding of the circulation with amino-acids is too great a physiologic load for

the liver to tolerate. Postmortem studies of nine patients who received substantial quantities of casein digest during their terminal disease failed to reveal evidence of toxic effects ascribable to the digests.

SUMMARY

(1) Nitrogen balance studies in 41 patients subjected to a variety of major surgical procedures revealed a net loss of nitrogen for the first ten-day period which varied widely from 3.81 Gm to 175.79 Gm in 36 patients. The loss was sustained for the most part during the first five days. In five instances, there was a slight net gain of nitrogen during the postoperative period due to early return to full diet.

(2) The most important factor in the nitrogen loss is the restricted ingestion of food combined with the general physiologic disturbances accompanying a major surgical procedure.

(3) Using the nitrogen balance as criterion, casein digest administered intravenously in proper proportion with glucose is effective in reducing or even preventing postoperative net loss of nitrogen and thus spares the organism from the effects of excessive protein catabolism.

(4) Casein digest and glucose intravenously may be employed as the sole source of nutrition, affording at least minimal caloric requirements under certain conditions, and include an adequate supply of amino-acids to maintain nitrogen equilibrium, or even afford a positive nitrogen balance in patients with depleted protein stores.

(5) Whether or not a surgical procedure is performed or contemplated, intravenous administration of casein digest is a means of forced nitrogenous nutrition.

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DISCUSSION —DR WARREN M. COX (Evansville, Indiana). I sincerely appreciate this opportunity to comment upon the papers by Doctor Brunschwig and Doctor Elman. As a biochemist, I cannot make any comment on their clinical observations. Our attention has been centered on the hydrolysate, its preparation, and more particularly its biologic utilization. Last week some of our studies in this regard were presented at the Federation meetings in Boston, and part of those may be of interest to this group.

We were particularly interested in the synthesis of serum albumin as effected by the intravenous administration of the casein hydrolysate. Others have made observations in this regard. Thus some years ago Doctor Elman made observations that regeneration would be effected both in animals and in a few clinical cases.

Doctor Madden in Doctor Whipple's laboratory made an observation that regeneration could be effected in dogs made hypoproteinemic by plasmapheresis, and Doctor Brunschwig showed his results in this regard this morning.

We were interested however in knowing quantitatively, whether the casein hydrolysate administered intravenously would have the same effect as casein or the hydrolysate given by mouth. For this purpose we followed the procedure of Weech in which dogs are made hypoproteinemic by low protein diet. They are fed this diet for three weeks. Following this, they are given protein at an intake level of 2.5 Gm per kilo and caloric intake level of 80 per kilo for a period of one week. The amount of regeneration during this one week's period constitutes the measure of efficiency of the protein.

Thus, we fed one group of dogs the casein hydrolysate by mouth and another similar group the casein hydrolysate by vein. The material was given in 10 per cent solution in sterile form and if we may have the first slide we can see the results.

(Slide) The albumin values are given in the first column on the left. This column gives the decline of serum albumin during the standardized depletion period. Here we have the regeneration when the material was given intravenously and here is the assay value as employed by Weech. You have an average assay value for the casein hydrolysate given intravenously of 0.43. By mouth—this is really a total of 21 animals—you have a regeneration average of 3.5. These figures are in entire agreement with the values previously reported for casein by mouth so that we can say that casein and casein hydrolysate by mouth and casein hydrolysate by vein have the same effect on serum protein regeneration.

In conclusion I think we might say that this means that casein hydrolysate by vein has about the same effect as beefsteak by mouth.

DR OWEN H. WANGENSTEEN (Minneapolis, Minn.) Owing partly to the work of Doctor Ravdin of this Association and to Dr. George H. Whipple of Rochester, N. Y. the attention of all of us has been focused on the great importance of meeting or attempting to meet the protein requirements of the surgical patient. It remains however for Dr. Robert Elman of this group to indicate that it is feasible and practical to maintain satisfactory nitrogen equilibrium with the administration of amino-acid.

Those two Danish observers, Henrique and Anderson, I think just prior to the last war showed that in a goat that casein hydrolysate could be utilized to advantage in establishing nitrogen equilibrium.

I think most of us with any experience at all know that you can inject practically without any reaction and that it would be fair to say that surgeons have been quite remiss in their attitude toward the feeding of surgical patients. I think in a sense physiologists have contributed to this dereliction or delinquency of ours in that they have not only pointed out but have emphasized that periods of starvation may not only be well-borne but some have affected to believe that in such periods of starvation mental and even physical efficiency are improved.

Anyone who has given the matter serious concern with reference to surgical patients will understand there is a difference. We are dealing with ill patients. We are dealing with patients who perhaps come to us from periods of starvation and we as surgeons now owing to the stimulation the problem has had from Ravdin, Whipple, Elman and others affect to manifest an interest in the problem. Our performance, in a sense, belies that manifested or professed interest for we do not begin to meet caloric requirements of patients or nitrogen requirements. I think most of us have been content to meet water and electrolytic requirements only. I contend that in the immediate future surgeons must have an eye to meeting not only water and electrolytic requirements but also those of calories, nitrogen, mineral, and vitamin requirements.

The magnitude of the problem imposed upon the surgeon in trying to do this is manifest in these slides that have been shown you by the two preceding speakers.

My associates and I, as Doctor Elman said, are interested in the problem of trying to maintain nitrogen equilibrium with human plasma. More than two years ago we published a paper indicating that nitrogen balance could be maintained in such a manner. Perhaps it is necessary to point out that there is a fundamental difference in behavior when plasma is injected intravenously and when amino-acid is injected. When one uses protein plasma and the nitrogen intake of the urine is reduced to a low level through the use of glucose ingested by mouth or given intravenously there is no augmentation of excretion of nitrogen in the urine. All the plasma given intravenously is available for storage and you quickly raise the level of plasma protein.

On the contrary, when one injects amino-acids, only so much of the amino-acids are available for energy requirements, unless calories are given in large quantity, that you have to inject larger amounts. So the matter of dosage comes in. I suppose it would be fair to say that for a man who weighs 70 kilos an optimum requirement of protein in the order of magnitude of something like 70 Gm is necessary to maintain nitrogen equilibrium.

There are many practical problems involved in this issue. It is obvious, of course that we are dealing essentially with starved surgical patients. Patients with obstruction to pyloric outlet present an ideal problem about which to discuss this situation.

In our own clinic, now for more than two years, we have done no two-stage operations in such patients. We have only done one-stage operations, feeding the patient intravenously with glucose and amino-acid and plasma. I do not believe that glucose is the ideal solution. I hope sometime we will have an agent by which we can administer the required amount of calories and not thrombose the veins, as we are likely to do in using 20 per cent glucose and not give too much fluids and overhydrate our patient, if he is very old, and lose him through the agency of pneumonia and cardiac failure.

I think the papers are very pertinent and it is a subject in which we will all have to manifest a greater interest.

DR HARVEY B. STONE (Baltimore, Md.) I should like to ask Doctor Elman whether he will enlighten me in closing on one point. Does the administration of these protein split products which may be used for regeneration, as I understand it, either of the tissue proteins or of the serum of the plasma proteins, exert the same osmotic pressure when administered as the administration of plasma does? In other words, will it serve the same purpose in the physiochemical maintenance of fluid balances between tissue spaces and circulation that can be expected from the administration of serum plasma?

DR ALEXANDER BRUNSCHWIG (closing) There is just one more point I would like to emphasize. In our experience we have found what we think is one absolute contraindication to the injection of casein digest and that is icterus or marked liver damage, as being discovered by appropriate liver function tests. We attempted to build up, so to speak, three icteric patients showing carcinoma of the pancreas; the icteric indices in these patients ranging from 40 to 120 and in each case a very severe chill and rise in temperature, which promptly dropped in a few hours, occurred. The patients felt very uncomfortable. Their appearance was quite alarming at the time.

In another patient a chronic alcoholic, who had no icterus, but whose liver function, by the hippuric acid test, was very low, there was also a very severe reaction.

Apparently the liver when it is abnormal cannot cope with a flooding of the circulation by amino-acids and this reaction results.

We have observed, however, that a patient who will exhibit the reaction as a result of intravenous injection does tolerate subcutaneous injections very well without reaction. In our experience a 3-3 per cent solution of casein digest in distilled water can be given repeatedly day after day, just as one would give isotonic saline or 5 per cent glucose.

We have also observed that in patients in whom the liver function test is very low and who did exhibit a reaction resulting from one of the injections of casein digest, when the hepatitis improved to some extent they could tolerate intravenous injections. One patient who had an icteric index of over 80 and in whom we did not want to risk an intravenous injection subsequently received intravenous injections after the icteric index had been normal for about two months, without any untoward effect.

DR ROBERT ELMAN (closing) It has, of course, been quite impossible to touch on anything but the bare essentials of all the implications of the new method of therapy.

In answer to Doctor Stone's question these amino-acid mixtures have osmotic pressure which is similar to that of glucose. Therefore in order to exert the same colloidal pressure as protein they would have to be synthesized in the serum protein. But the matter is not as simple as that because we have observed on many occasions a very pronounced diuresis, a passage of fluid from edematous intestines, in intestinal obstruction, etc. following the injection of amino-acids, without very much significant increase in the serum protein concentration. We have been tempted to believe that the amino-acids

NITROGEN LOSS

in some way lead to an increased nutrition of the tissues, perhaps the capillaries, which enable the food to flow in the right direction, namely, into the lumen of the blood vessels and out through the kidneys, and relieve the edema of various body tissues.

It seems sort of presumptuous to bring up this point again, which has been emphasized by Doctor Wangensteen namely, that food is important for life, and yet we see patients on surgical wards being given all sorts of vitamins because of the emphasis and the publicity they have received, and yet many of them are starving to death.



AIR-RAID SHELTER PROPHYLAXIS

A method of prophylaxis which, we are informed, may be introduced into the shelters can be properly commented upon by a surgeon—namely, the provision that has been made for the wearing of masks to prevent the spread of droplet infection. We are told that half a million masks are ready to be distributed as and when required. Surgeons have long acted upon the view that infection can easily be transferred by means of the breath, and the wearing of masks is a routine in the operating theatre. The human nasal and pharyngeal mucosa is in some cases as susceptible to infection as an open wound, and I have often been surprised that physicians have not strongly preached and by force of example demonstrated that contagion of the common influenzal cold could be prevented by the wearing of an efficient mask. If in the shelter why not in the work-room or office? Making the reasonable assumption that in Great Britain every year one million people lose one day from work as the result of a cold, the time lost from this cause annually would equal nearly 3 000 work-years. Would it not be worth attempting to reduce this time by mask prophylaxis?

—V Zachary Cope M D British Medical Journal

SYMPOSIUM ON BURNS

CLINICAL AND EXPERIMENTAL STUDIES WITH THE KOCH METHOD OF TREATMENT OF HEAT BURNS*

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THE PURPOSE of these studies has been an effort to determine the effect of primary pressure dressings upon the loss of plasma from the burned area and into the surrounding tissues

CLINICAL STUDIES

In our approach to the clinical problem we have, like Koch and many others,^{1 2 3 4} regarded burns as badly contaminated serious wounds and, in the preparation of the patient for the dressing, have employed the fundamental surgical principles which many of us have advocated for the treatment of wounds in general. However, for a proper evaluation of these studies it seems to us best to describe in some detail the exact procedures we have followed

Preoperative Period—This is devoted to an assay and treatment of the patient's general condition and an effort to lessen further contamination of the wound. At the site of the accident or in the first-aid stations we try to prevent the use of ointments, oils and various "home remedies" by advocating the use of a dry, clean sheet, piece of cloth, or a towel when dry sterile dressings are not available. The patient should be kept warm with blankets under and over him. Hot drinks in small amounts may be given. Morphine in adequate amounts to produce sedation is given as soon as available. The patient is taken to a hospital as soon as possible.

In the hospital all persons connected with the care of these patients should be properly capped and masked. A rapid survey and physical examination is made without disturbance of either the patient or the dressings. In extreme cases we have administered oxygen during this period.

As soon as possible a 2 cc heparinized blood specimen is sent to the laboratory for hematocrit† and plasma protein determinations. These initial values are considered the base line. If the burn, however, is a serious one,

* Read before The American Surgical Association, Cleveland, Ohio, April 6-8, 1942

† The method employed for the hematocrit determination is that advocated by Guest and Siler⁵. As mentioned, 1-2 cc of heparinized blood is sufficient for both hematocrit and plasma protein determinations. From this vial of blood, thin-walled capillary tubes in pairs are partially filled. One end is sealed in a microflame and the tubes thus filled and sealed are centrifuged in a special carriage until the cells are packed to a constant

that is, 25 per cent of body surface or more, we do not wait for the laboratory report, but immediately expose a vein in some unaffected site, usually the ankle, and start plasma transfusion. Our experience is that one-half normal plasma given by intravenous drip is best in the early stage of the injury. Only in very rare instances have we seen a burn of such magnitude that a

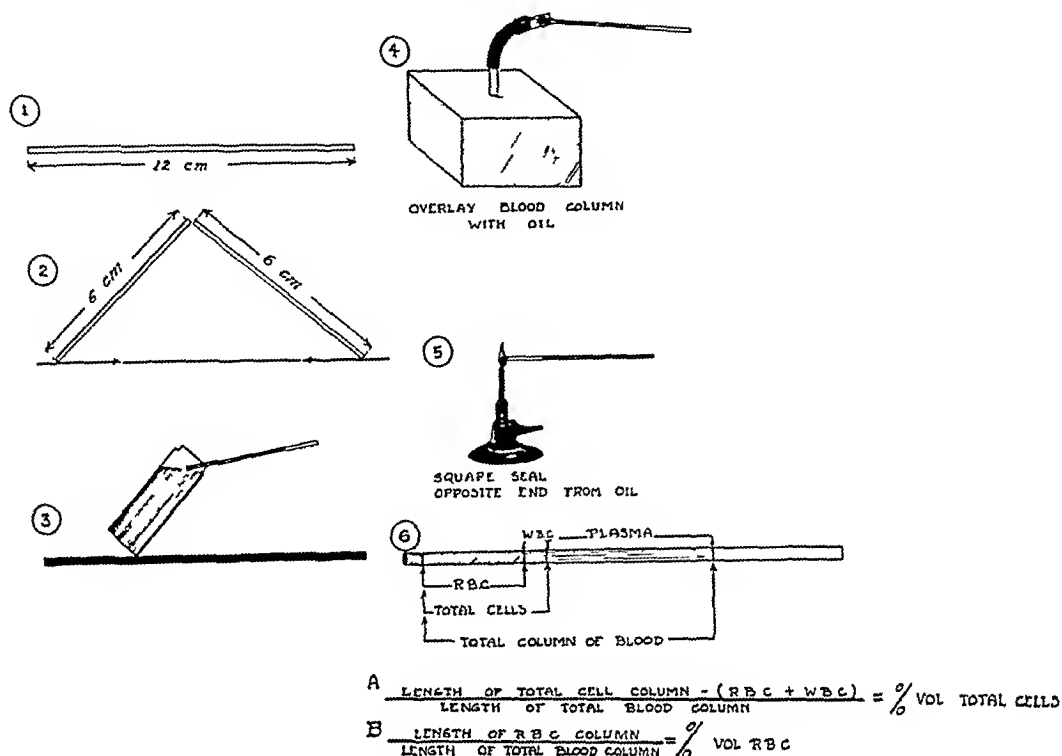


FIG. 1.—Diagrammatic sketch showing the technique for capillary hematocrit determination (1) A 12 cm capillary tube (2) Same tube divided into two 6 cm capillary tubes (3) Capillary tubes filled two thirds full with heparinized blood (4) Method of placing paraffin oil over blood column to prevent evaporation of plasma (5) Technic for sealing open end of capillary tube (6) Capillary tube after centrifugation. Measurements made by microscope equipped with graduated mechanical stage (A) Calculation for per cent volume of total cells (B) Calculation for per cent volume of RBC

site for venous cannulization could not be found. When this does occur one is certainly justified in giving intraarterial plasma transfusion, a route sometimes forgotten. When we feel that the condition of the patient will permit it the second phase of treatment is begun.

The columns of cells and plasma are then measured by means of a microscope which is equipped with a cross-hair eyepiece and a graduated mechanical stage. From these measurements the volume of "total" cells and "red blood cells" are calculated in percentage of whole blood (Fig. 1). The principal advantages of the capillary hematocrit method are that it is economical of blood, that the anticoagulant used does not affect the size of the cells, that the volumes of red cells and white cells may be read separately with ease, that errors due to rubber sealing devices are avoided, and finally that it is rapid. The entire procedure including calculations requires less than ten minutes. This is a particularly important factor in the treatment of "thermal shock" and also important to the technician who may be required to do as many as 20 to 30 such determinations daily.

While the hematocrit tubes are being read the remaining 1-2 cc of heparinized blood is spun in a special angle centrifuge head. From this plasma a protein determination is obtained using the Guthrie modification of the Barbour-Hamilton "falling-drop" apparatus. This procedure requires five to eight minutes.

Operative Treatment—In this stage of the management of burns an effort is first made to convert a contaminated large wound into a clean wound. The patient is placed on the operating table upon a sterile sheet. In most instances general anesthesia is administered. Intravenous therapy is continued as indicated by the general condition of the patient and the laboratory tests. The surgeons and nurses, who have been gowned and gloved in the usual fashion, after scrubbing for ten minutes, drape the involved region with sterile towels and sheets. The wound is gently but thoroughly washed with white soap and water. The soap is irrigated from the area with physiologic saline solution. Gross débridement is carried out during this procedure, that is, all of the necrotic skin and blisters are removed. The surgical team changes gown and gloves, after which the area is redraped. Using fresh instruments and containers, a more minute debridement is now done and the wounds are gently washed with white soap and water the second time. Irrigation is again carried out with physiological saline solution.

The pressure dressing is then applied as follows. The wound is first covered with sterile fine mesh single thickness vaselined gauze strips on top of which are placed flat gauze dressings followed with fluffed sponges. Pressure is exerted upon the area with a folded gauze roll. Further compression is obtained not only upon the wound itself, but also upon the surrounding tissue by placing sterile "mechanic's waste or cotton" over the entire region. The latter is held in position with a sterile muslin roll. The dressing is made a complete surgical one by means of adhesive tape which maintains the pressure and aids in immobilization of the involved part. If necessary, either sterile aluminum splints are incorporated in the dressings as in the case of an involved forearm or hand, or immobilization of the lower extremity is maintained by the application of light plaster encasements. This dressing is allowed to remain untouched, usually, for from ten to fourteen days. In the case of first- and second-degree burns the wound should be completely healed when the dressings are removed, while in the case of third-degree burns, the wound usually allows the application of a split-thickness graft, as advocated by Blair and Brown. If there is mild infection of the granulating wound, postage stamp Thiersch grafts may be safely applied. In the rare instances of gross infection, the wound must be further prepared for grafting by suitable means.

Postoperative Care—Since no further care of the wounds is necessary for a long period of time, the main problems are concerned with the treatment of the patient's general condition and good nursing care. In the severe case, a continuation of all the laboratory tests and therapeutic procedures, utilized preoperatively, may be necessary for several days. We refer particularly to the use of the hematocrit, specific gravity and plasma protein determinations of the blood for the control of fluid and plasma therapy.⁶

Results—We have, during the past two years, used this method of primary cleansing, compression, and rest treatment of burns on 134 patients. Of this number, 90 were children and 44 were adults. From the standpoint of the

extent of the burns, as measured by Berkow's method, the cases may be divided as follows Less than 15 per cent of body surface, 39 cases, 15 to 30 per cent, 58 cases, 30 to 60 per cent, 27 cases, 60 to 85 per cent, nine cases, 85 per cent or over, one case (Table I)

TABLE I

NUMBER OF CASES TREATED IN THIS SERIES REGARDING PER CENT OF BODY SURFACE INVOLVED AND DEPTH OF BURN

Depth of Involvement	Degree of Burn	Per Cent of Total Body Surface Involved					Total Cases	Per Cent
		15% or Less	15%-30%	30%-60%	60%-85%	85% or More		
	1° and 2°	11	20	12			43	32
	3°	4	6	3			13	10
	1°, 2° and 3°	24	32	12	9	1	78	58
Total Cases		39	58	27	9	1	134	
Per Cent		29	43.8	20	6.7	0.7		100

In this series of 134 cases there were five deaths, or a mortality rate of 3.7 per cent. Of the five patients who died, three were given a general anesthetic and the other two were treated under analgesia. Among these three anesthetized patients the causes of the deaths were as follows. One, an adult, with a 40 per cent burn, died on the fourth postoperative day from a cerebral accident. Another was a child, with a 40 per cent burn, who died of asphyxia from laryngeal obstruction on return from the operating room. The third, who had a 60 per cent burn, died five hours after treatment. The exact cause of death is unknown, but was explained by a persistently high hemoconcentration in spite of large amounts of plasma therapy. No autopsies were performed upon any of these cases.

Two patients died who were treated under analgesia. One, an adult, with an 85 per cent burn, died on the fourteenth postoperative day from pneumonia, empyema and pericarditis. There was a left mild hydronephrosis from a mechanical ureteral blockage. Autopsy was performed on this case. The other, a child, had a 70 per cent burn, and died 12 hours after injury, in a state of hyperpyrexia. No autopsy was obtained on this case (Table II).

TABLE II

MORTALITY RATE AND ANALYSIS OF DEATHS IN THIS SERIES OF CASES

Total Cases	Deaths	Mortality Rate
134	5	3.7%

ANALYSIS OF DEATHS

Deaths	Per Cent Body Surface Involved	Time Survived	Cause of Death		Remarks
1	40	4 days	Extensive burn	Cerebral accident	Anesthesia
2	40	3 hours	Extensive burn	Asphyxia	Anesthesia
3	60	5 hours	Extensive burn	Not explained	Anesthesia
4	85	14 days	Extensive burn	Pneumonia-empyema-pericarditis	Analgesia
5	70	12 hours	Extensive burn	Hyperpyrexia	Analgesia

Clinical studies of the various wounds regarding infection has been most difficult. Carefully controlled bacteriologic studies were not available in this series of cases. Clinically, 79 cases had no infection, 15 cases were mildly infected, 25 cases were grossly infected, and in 15 cases the results are unknown (Table III). There were only a few minor infections in the

TABLE III
CLINICAL SURVEY OF THE WOUNDS AND INFECTION

	Degree of Burn			Total	Per Cent
	1° and 2°	3°	1° 2° 3°		
No infection	34	2	43	79	58.9
Mild infection	4	6	5	15	11.1
Gross infection	2	3	20	25	18.6
Result unknown	3	2	10	15	11.1
Total	43	13	78	143	100.0

first- and second-degree burns. In the third-degree burns, where grafting could not be done at the first dressing, the inevitable bacterial contamination of the granulating surfaces led to no serious local wound infections. There were no deaths due to infection, unless the one patient with an 85 per cent burn, who died 14 days after the operation from streptococcic pneumonia, empyema and suppurative pericarditis, had her portal of entry for these complications in the burned area.

Discussion of Clinical Studies—Although careful clinical and laboratory studies have been made upon this series of patients we are faced with the difficulty of not having a satisfactorily controlled series treated by any other method for comparison. In fact, the variation in individuals and the extent of burns as they ordinarily occur in accidents make it very difficult to run a parallel series with any degree of scientific accuracy. We have not attempted to do it. The advantages of this method of therapy must, therefore, be stated more or less in terms of clinical observation of the various doctors and nurses working in the department of surgery, many of whom have had considerable experience with other forms of therapy.

The decrease in the amount of suffering by this method of treatment seems to be very striking. Rarely is it necessary to continue to use morphine or codeine for more than a day or two after operation. The patients can move about much more easily. The nursing problem is greatly simplified. There is a great saving in the cost of dressing materials when compared with other methods which require frequent dressings or compress therapy. The temperature charts seem to us to show a surprisingly rapid return to normal levels.

Using "primary cleansing, compression, and rest treatment of burns," we have found, particularly in the case of children, as well as adults, that these patients rapidly assume their own water balance by oral fluid intake and that parenteral administration is only required in the more severe cases. These patients are given a high protein diet as soon as possible and it has been our experience that solid food is enjoyed early in their convalescent period.

It is our belief that the careful toilet of the wound, under anesthesia, and the long duration of the primary dressing markedly lessen the incidence of infection. The ease with which most of the patients can be restored to a normal physiologic state suggests to us that the pressure dressing may aid materially in preventing the loss of plasma at the site of the wound and into the surrounding tissues.

The dressings, as we have applied them, put the burned wounds at rest, and the healing, help prevent infection and promote the comfort of the patient.

At the present time we are running a series of burned cases in which a sulfonamide drug is used systemically, and occasionally locally, in addition to the Koch method of treatment. It is too early in the study to draw any definite conclusions. In the series reported in this paper no sulfonamide drugs were employed.

EXPERIMENTAL STUDIES

In an effort to avoid some of the pitfalls of uncontrollable clinical studies, it was decided to try to determine upon laboratory animals the effect of pressure dressings upon the loss of plasma in and about the site of burned areas. For this purpose it was decided to use dogs, even though they do not blister from burns as do humans.

After considering the problem of an attempt to find if there is any actual difference between a burn which has a pressure dressing applied on it and one which has not, we felt that the observations which could be controlled and measured more accurately than any other were the volume-per cent red cells of the blood and the plasma protein content. It should be clear that these two determinations do not attempt to measure the amount of plasma loss, but may indicate the degree of shift of water balance in the blood. It would follow then that these two determinations would be more indicative in a comparative study and more applicable to the phenomenon of "thermal shock" seen in man than perhaps any others.

METHOD

This study in burns utilized the principle of experimenting upon animals in pairs. Dogs were used, and they were paired as well as possible from the standpoint of equivalent size, weight, and health. All of the burned dogs were given essentially the same diets for at least two weeks before any observations were made.

At varying periods, for a week before the burning injury, blood samples were obtained upon which hematocrit and plasma protein determinations were made. All of these blood samples were taken at practically the same time of day. This gave us a fairly good base line as to their normal values for these two determinations. Usually the hair was shaved off of the entire back, abdomen and both hind legs the night before each experiment, and on the following morning the animals were placed and tied into position on the tables. Equivalent areas were then outlined with brilliant cresyl green

on each animal, after which the skin of both was cleansed with soap and water for ten minutes. This area in most instances represented between 15 and 25 per cent of the body surface. Anesthesia was induced by intravenous sodium nembutal. A gas-oxygen flame was used to burn the animals. This flame was kept at a constant length, and the burner was kept at a relatively constant distance from the skin of each animal. Each pair of dogs was burned for the same period of time as determined with a stop watch.

On one dog a pressure dressing was applied to the burned area and to the surrounding soft tissue, similar to the pressure dressing which we have used in the clinical treatment of burns. After application it was enclosed

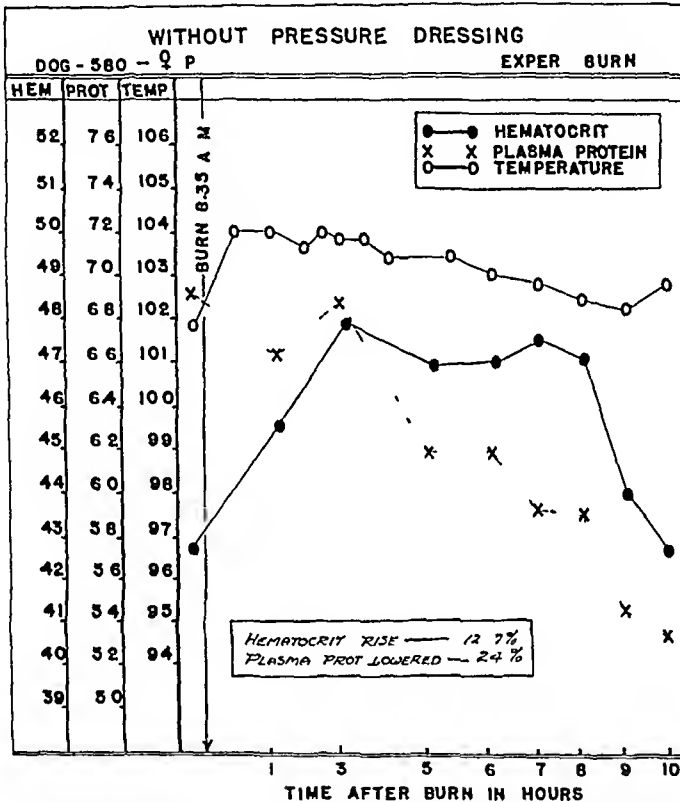


CHART 1—Representative graph of hematocrit and plasma protein observations in an animal *without* a pressure dressing over the burned area

in a light plaster encasement so that the animal could not disturb it. On the other hand, the second animal received no dressing at all. We believe that this procedure represents a fairly good approach to the problem of producing equivalent degrees of injury in two experimental animals.

Before the experiment was begun each animal had a sample of blood withdrawn for hematocrit and plasma protein determinations. After the animals were burned blood samples were taken every hour for three hours, and then every two hours, until a total of eight such specimens were obtained. We found that this method of blood sampling was sufficient to cover the maximum degree of hemoconcentration thus obtained. Also, the tem-

perature, pulse, and respirations were observed before burning and at the time each sample of blood was drawn

A group of 12 animals, or six pairs, were observed in this study. In these experimental animals a degree of hemoconcentration was seen in all cases and, as would be expected, the plasma protein was lowered as the former rose. In an analysis of the paired animals, that is, comparing those animals treated with pressure dressings versus those animals without dressings, several generalizations can be made. In practically all instances the degree of hemoconcentration was greater in the animal without a dressing than those which received pressure over and around the site of injury. An-

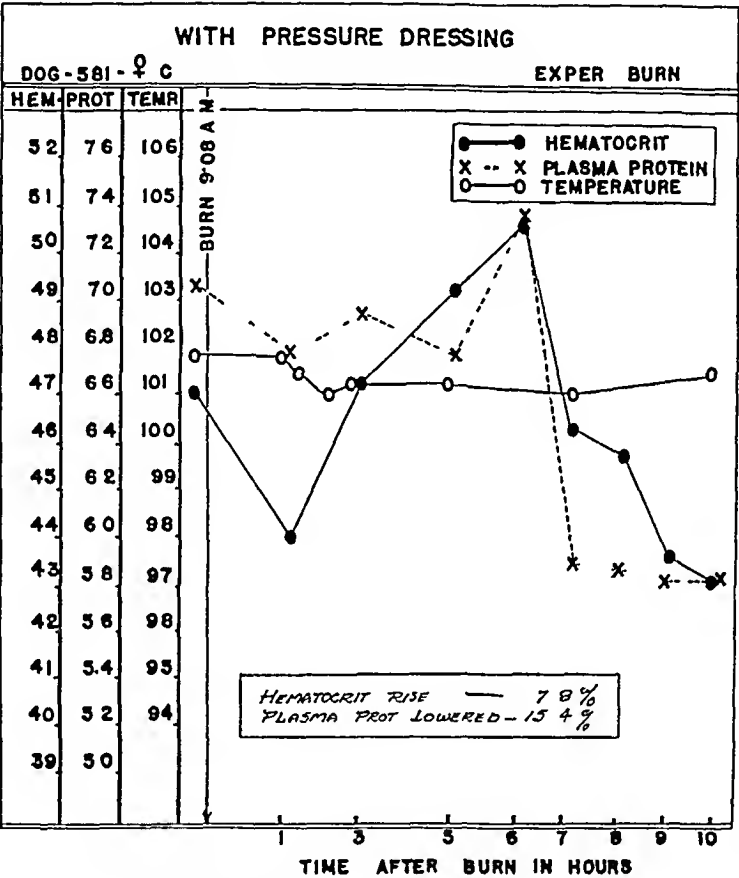


CHART 2—Representative graph of hematocrit and plasma protein observations in an animal with a pressure dressing over the burned area

other interesting fact is that the rate of hemoconcentration occurred more rapidly in the group without a pressure dressing. The maximum point of hemoconcentration was reached usually two to three hours after sustaining the burn. A representative example is shown in Chart 1. In the group of animals with pressure dressings the rate of hemoconcentration was slower, with the maximum point usually observed four to six hours after the injury (Chart 2). These observations suggest to us that pressure over and around the site of injury mechanically suppresses the rate of plasma loss.

A more careful study of the two composite groups was done. To submit the results to biomathematical analyses we felt that it was more just to use

the percentage change in the hematocrit determinations of the two groups rather than the actual figurative change. The method of statistical analysis used was the "t-test" of Student.⁷ In this test "t" is the difference between two means divided by the standard error of that difference. On analysis (Table IV), it is revealed that such a change in the hemoconcentration,

TABLE IV
STATISTICAL ANALYSIS OF THE MAXIMUM HEMATOCRIT CHANGE IN EXPERIMENTAL BURNS

Burns Without Pressure			Burns With Pressure		
Pair No	% Diff	(% Diff)	Pair No	% Diff	(% Diff) ²
1	28.3	801.0	1	18.9	355.8
2	17.2	296.7	2	2.3	5.4
3	3.6	13.2	3	15.4	238.5
4	5.5	30.2	4	0.2	0.04
5	34.5	1187.4	5	17.9	320.9
6	16.9	284.7	6	3.7	14.0
6	105.9	2613.1	6	58.5	934.7
Mean %			Mean %		
17.6			9.7		
S = 10.5			P = 0.2		
t = 1.304					

The significance of these observations was determined by use of the formula devised by Student.

observed with and without pressure, could occur 20 in 100 times, due to chance alone. To be significant it must be five or less times in 100, due to chance. This assay does reveal that the pattern of response is more regular in those burned animals with pressure dressings than those without pressure.

Other observations suggest that the dogs with pressure dressings suffered much less "thermal shock" than those without dressings. In the former group the temperature generally did not go so high, and the pulse rate did not show the degree of increase as did those dogs in the latter group. Furthermore, we observed that the dogs with pressure dressings appeared to be more comfortable, generally, than the dogs without dressings. The tendency was for them to move about and take fluids without a great deal of discomfort.

There are some very definite reasons why we are not attempting to analyze and discuss the degree of hypoproteinemia in this experiment. In the first place the exact mechanism of balance between the protein content of the blood and of the tissue is not too well understood at this time. Moreover, as plasma protein is lost the mechanism of drawing upon protein reserve of the tissue is not known, and until further investigation clarifies this phenomenon we must be satisfied to accept protein determinations at face value, that is, that the protein determination represents the amount present in the circulating plasma when the sample is withdrawn.

These animal experimentations suggest that pressure on and about a burned area may inhibit the rate and degree at which hemoconcentration occurs, but do not conclusively prove it. We realize that a great many factors enter into this problem and that more research must be done before

definite conclusions can be reached. Some phases of this study are now being done.

Discussion—In the untreated burns hemoconcentration was obtained on an average of two to three hours after the injury, while in the dogs where a pressure dressing was applied it occurred on an average of four to six hours after the injury.

The mean per cent of hemoconcentration was 17.6 in the untreated animals, and 9.7 per cent in the animals with pressure dressings. This average per cent difference would suggest that pressure on and about a burned area is beneficial in preventing hemoconcentration, yet on statistical analysis it is not significant.

The circulating plasma protein was lowered in about the same ratio as hemoconcentration occurred. As stated elsewhere, we have not attempted to analyze this change since the relationship between circulating plasma protein and the protein reserve in the tissues is not known and apparently variable.

CONCLUSIONS

(1) Our clinical and experimental studies suggest that primary pressure dressings may reduce the loss of plasma at the site of, and into the surrounding tissues of, burned areas.

(2) The capillary hematocrit method was used for determining the hemoconcentration in both patients and animals. It is very rapid, requires much less blood, and is, we believe, more accurate than other methods generally employed.

(3) With this form of dressing, hemoconcentration may be delayed and perhaps is less severe.

(4) The drop in plasma proteins was definitely less in the dogs treated by pressure dressings than it was in the controlled animals. The significance of this may be open to question, inasmuch as the balance between the tissue proteins and the circulating proteins is not well understood.

(5) It appears to us that the pathologic-physiologic changes resulting from burns is less severe and more readily controllable under this form of therapy than by other methods employed. Certainly the patients are more comfortable and more easily cared for. The incidence of infection has been relatively slight.

(6) What effect the use of sulfonamides in the treatment of burns will have, systemically and locally, in addition to the procedures described, has not yet been determined. It appears certain that they will aid materially in further controlling the infection.

(7) In conjunction with cleansing and débridement of the burned area we have used the method of primary pressure dressings as described in this paper upon 134 patients. The mortality rate was 3.7 per cent.

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DISCUSSION —DR WILDER G PENFIELD (Montreal, Canada) I want simply to call attention to the fact that the subject of burns is a most timely one at the moment During the last Autumn I had the opportunity to go to Great Britain to make some sort of survey of clinical surgical problems there for the Canadian Research Council, and during that trip I had the opportunity of being in the general hospitals and in the military hospitals, British and Canadian

My own reaction to the clinical problems was that burns are the outstandingly important problems There are a good many burns now, of course, because of the fact that there are burns from bombs because very frequently in open fireplaces the contents of the fireplaces are driven out into the faces of people sitting about them, because of the use of incendiary bombs and because of flash burns on all the surfaces But it seems quite likely that all of the surprises that are to be sprung in this war have not yet appeared It is possible that the forces may be called upon to deal with chemical burns to deal with flame burns of a different type and the need of surgeons who have the material in their hands of voluntarily directing their attention to this problem is a great one The simple problem of early recognition of a third-degree burn the question of whether tanning increases the depth of the initial burn, the problem of the control of pain and of course the problems of shock infection, toxemia, scarring, wound healing, all come into the picture But what is needed is not a council of perfection in the treatment of burns What is needed is standardized simple methods which could be used by a man in a dressing station who has 5 or 50 burns to treat at once, methods that can be used in hospitals that might have to treat hundreds of them

DR SUMNER L KOCH (Chicago Ill) I am delighted to have an opportunity to hear these papers because it seems to me never has a presentation been made that has stressed so clearly and emphatically the application of sound surgical principles to the treatment of a difficult problem Doctors Siler and Reid have done that They have emphasized first of all the careful cleansing of the open wound without adding further contamination and further infection second, the application of a dressing that does not add injury that does not cause a further destruction in addition to that which has been sustained third, the value of pressure a factor in wound healing which was emphasized years ago by Doctor Blair, which was forgotten, remembered, and now is being utilized to help wound healing fourth, Doctor Siler has suggested limiting the important fluid loss, and fifth, putting the part at rest

These are sound surgical principles They are going to live if they are sound, and it seems to us they are definitely applicable

We have been using that method at the Children's Hospital, the Cook County Hospital and for a period of three years, beginning January 1, 1939 we have used the method exclusively During that period of time, with the help of Dr Harvey Allen who is now at Camp Custer, and of some splendid residents who are now in the Army and Navy we were able to care for 485 hospitalized cases with severe burns The mortality in that group was 19 cases, or 3.9 per cent a little higher than the mortality that Doctor Siler and Doctor Reid have And all the other things that could be said concerning the ease of care, the lessening of hospital morbidity, etc, were observed in these cases also

Now, without wishing for a moment to answer for Doctor Siler or Doctor Reid the question that Doctor Penfield suggested, we had a discussion in Chicago on this problem of burns and Captain Cook said "Well, that method might work splendidly in a hospital where you have every help and available resources It will not work at all

in the field " We tried to say that the method, or something analogous to it, would work If men were simply instructed, first of all, to mask themselves and not add infection, and then to put a preparation, an exact preparation we will not pretend to describe, over these open wounds, consisting of an oily dressing containing a sulfonamide, such as Doctor Dragstedt, and his associates, used at the University of Chicago Then over this dressing, which could be applied with sterile spatula very rapidly, a compression dressing and a splint were applied, it seemed to us that such a method might be used in a large group of cases, and thus be made fit for transportation When the opportunity arose, they could be treated by this more definitive method of treatment that Doctor Siler has described so well

DR LEO ELOESSER (San Francisco, Calif) This discussion has centered largely upon variations on an old theme, namely, the variations in the various applications of antiseptics I wonder whether in third-degree burns, leaving quite aside the first- and second-degree burns we are not standing still as we were standing in the era before the debridement of wounds The question that Doctor Penfield has brought up is very important—could something be done for third-degree burns where they are not received in too great numbers, especially for burns of the face and hands as it is to other wounds, namely, an early debridement and an attempt to convert what is certain to become a more or less septic wound into a surgically aseptic wound I think perhaps if we could debride earlier wound lesions, especially of the hands and face, and immediately skin graft these surfaces we know are doomed to destruction, perhaps the complications which we have been discussing this morning might be avoided

I merely put that question to you for your consideration I think that in a few cases those methods are applicable As Doctor Penfield says, when many of them are received at once, the method is too time-consuming to be used widely, but where not many of them are received, then I think it is useful

DR VINTON E SILER (closing) Apropos of Doctor Young's talk, I would like to say that we have not proposed this I am sure Doctor Koch has the ideal method It may be just the compromise between the simple procedure and the ideal



SCIENCE AND HUMAN PROGRESS—III

Entomology and Survival

ENTOMOLOGY, devoted to the study of insect life, has already greatly aided humanity to win the bitter struggle against the vast hordes of insects competing for our food supply A most striking illustration of the effective work of entomologists is the recovery of the continent of Australia from threatened depopulation by the swift spread of a fast-growing cactus A million acres of valuable land were being occupied annually by cacti in an advancing wave no ordinary measure would stop The entire continent was in danger of being engulfed, as sixty million acres had been, when entomologists suggested employing an insect which lives only on cactus plants The *Cactoblastis cactorum* was finally brought in from Central America and by virtue of its prodigious appetite and enormous fecundity Australia has been saved for Man

—A Cressy Morrison, Transactions of the New York Academy of Sciences, Series II, 2, No 3, January, 1940

INFECTED BURNS WITH HEMORRHAGE*

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OCCASIONALLY chronically infected burns show a decided bleeding tendency which seems to resist all forms of topical and general therapy. Although infection is a common complication of cutaneous burns, hemorrhage is relatively rare, occurring in approximately 2 per cent of the cases.¹ Gunn and Hillsman² state that hemorrhage occurs in only a small percentage of cases, and is usually met with only in dirty, sloughing, badly infected burns. Da-Costa mentions that the raw surface, resulting from separation of sloughs in deep burns, is slow to heal, and may be complicated by hemorrhage.

If the infected burned area is extensive, the prolonged and uncontrolled bleeding results in a major therapeutic problem. The constant loss of blood soon produces a marked anemia and subnormal serum protein level, in spite of frequent blood transfusions. The absorption of septic bacterial products causes a continued septic fever with frequent chills, rapid pulse, prostration, and increasing debility. The patient's mental depression and the marked tendency to develop contractures further complicate an already difficult problem. A vicious cycle becomes established—the more the patient bleeds, the greater the infection becomes as a result of the anemia, low plasma proteins and debility, and the greater the infection becomes, the more the patient bleeds.

In the three cases of chronically infected burns which we are reporting, the bleeding was characterized by a continuous diffuse ooze of blood over long periods of time, up to five or six months. The local use of lanolin or vaselined pressure dressings and various topical applications of such solutions as boric acid, Burow's, Dakin's, azochloramide, dilute acetic acid, mercuriochrome, hydrogen peroxide, silver nitrate, and 1 per cent copper sulphate failed to bring the bleeding under control. The administration of sulfonamides orally in two, and locally in one of these patients, was likewise unsuccessful. In each instance, however, the application of a water suspension of activated zinc peroxide dramatically stopped bleeding within 24 to 48 hours.

CASE REPORTS

Case 1—Our attention was first attracted by this hemorrhagic tendency in the case of R. C., white, male, age 24, who was admitted to the Holmes Hospital, November 22, 1940, with an old infected electrical burn of his back of six years' duration. The infection was chronic and recurred frequently in spite of repeated radical excisions and many types of treatment. At the time of this admission, an ulceration three inches in diameter was present in the burn scar over the center of the lower back. The infected granulation tissue exhibited a persistent bleeding tendency which previously had

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942.

not been controlled by Dakin's, azochloramide, copper sulphate, saline boric acid hydrogen peroxide or specific bacteriophage solution locally. Lugol's solution and sulfanilamide by mouth also were ineffective. His red blood count progressively fell to a level of 2,800,000, with a hemoglobin of 9 Gm. His bleeding time, blood platelet count and prothrombin time were all within normal limits.

Bacteriologic study of the wound showed presence of an aerobic hemolytic staphylococcus and an anaerobic nonhemolytic streptococcus. It was thought that this case probably represented a type of chronic cutaneous ulceration, as described by Meleney. Caustic excision of the infected area followed by daily dressings with zinc peroxide was done, and the bleeding was promptly controlled. As soon as the zinc peroxide was discontinued and another solution, such as Dakin's, was employed, the bleeding promptly reappeared. The reapplication of zinc peroxide again quickly stopped the loss of blood.

After the effective control of the infection and bleeding, the clean granulating area was then successfully grafted by means of pinch-grafts followed in 12 hours by continuous zinc peroxide dressings. The patient was discharged March 3, 1941.

Case 2—T. R., white, male, age 48, received second- and third-degree burns of the legs, thighs, arms, and hands, November 2, 1940. While using an acetylene torch to cut metal, a can of gasoline nearby became ignited, which, in turn, ignited the patient's clothing. He was admitted to the Dermatologic Service of the Cincinnati General Hospital one hour after injury. Treatment consisted essentially of continuous dressings of Burow's solution, bed rest, and general supportive measures. Fifteen days later, it was noted that the patient had developed infection of the burned areas.

When he was transferred to the General Surgical Service for treatment and grafting, December 3, 1940, it was noted that the burned areas on both legs were bleeding. After continuous compresses with Dakin's solution, postage stamp Thiersch grafts were applied to the granulating wound. The grafted areas soon broke down and the wounds continued to bleed. Many types of topical therapy were then tried but all failed to stop the bleeding. Among the solutions used were saline, boric acid, acetic acid, azochloramide, cephrin chloride, mercurochrome, Dakin's solution and hydrogen peroxide. In spite of frequent blood transfusions, the anemia became more and more pronounced. He received daily 24 ounces of orange juice and 75 mg. of cevitamic acid, without influence on the bleeding.

On April 10, 1941, the patient was shown in surgical ward rounds, and at that time he appeared obviously and chronically ill. The burned areas on both legs were covered with large masses of dark partially clotted blood and pus beneath which the granulation tissue was piled up and edematous (Fig. 1 A). Active continuous oozing of dark blood could be seen.

The patient was debilitated, discouraged, and disfigured by contractures of both legs. The temperature was 100–102° F., and of the septic type, pulse 100–130. *Laboratory Data*: RBC 2,300,000, hemoglobin 8 Gm., serum protein 5.7 Gm. per cent, serum albumen 2.5 Gm. per cent, serum globulin 2.2 Gm. per cent, hematocrit 31 per cent. The prothrombin time was 93 per cent and the blood platelet count was 260,000. After four and one-half months of unsuccessful effort to control the bleeding, the loss of blood became so alarming that bilateral amputation of the affected legs was strongly considered as a last resort.

Careful cultures of the wounds at that time revealed the presence of nonhemolytic *Staphylococcus albus*, hemolytic *Staphylococcus aureus*, and a nonhemolytic streptococcus. No strictly anaerobic bacterium was demonstrated.

On the basis of our experience in the former case, the local use of zinc peroxide seemed indicated, even though no strictly anaerobic or micro-aerophilic bacteria were present. In addition, the legs were straightened and slightly elevated by means of traction applied to Steinmann pins inserted through the os calcis.

Twenty-four hours after the first application of zinc peroxide suspension the bleeding was completely stopped (Fig. 1 B), and the granulation tissue was beginning to assume a bright red, healthy appearance which became more pronounced daily. Multiple whole-



FIG 1—A Bleeding granulation of infected burn of Case 2
B Appearance of granulation tissue 24 hours after first application of zinc peroxide suspension showing complete arrest of bleeding C Same wounds after skin grafting and healing

blood transfusions were given, and within two weeks the patient looked much improved, his RBC was then 4,000,000, and his temperature had fallen to approximately normal. The wounds were pinch-grafted in five sittings, between the dates of May 1, 1941 and



FIG 2—A Bleeding granulation tissue of infected burn in Case 3 B Same wounds after skin grafting and healing

July 15, 1941, because of the extent of the involved areas. By August 25, 1941 all wounds were healed except several small crusts, and only at this time was zinc peroxide therapy stopped. He was discharged November 1, 1941, completely healed (Fig 1 C).

Case 3—M L, white, male, age 13, was admitted to the Children's Hospital, June 13, 1941, 17 days after having received second- and third-degree burns of both lower extremities and his right forearm. While playing with a small fire, gasoline was thrown by him into the fire. The ignited fuel exploded on his trouser legs, and in removing these, he burned his right forearm. He was carried immediately to another hospital where the wounds were cleaned and sprayed with tannic acid. During the first week infection occurred beneath the eschar and it was, therefore, necessary to remove a great part of the crust. Warm saline compresses were then applied. At this time he

was seen and treated on the Surgical Service of the Children's Hospital. His temperature was 105° F, and of the septic type. Urinalysis was essentially negative. R B C 3,560,000, hemoglobin 9.1 Gm per cent. The wounds were treated with warm saline compresses followed in three days with Dakin's solution. The granulations rapidly attained a healthy appearance, but the patient still ran a septic course. The wounds were grafted June 24, 1941, July 17, 1941, and August 7, 1941. By September 7, 1941, 30 days after the last grafting, the granulations were bleeding quite freely and piling-up thickly about the now disappearing grafted skin. A donor area from the left thigh reacted similarly, being obviously infected. The patient was very pale, discouraged and disfigured by flexion contractures and large bleeding infected wounds of both legs (Fig 2 A). R B C 3,100,000, hemoglobin 7.4 Gm per cent, hematocrit 23 per cent. Many solutions were used unsuccessfully, including acetic acid, saline, boric acid, azochloramide in olive oil and lanolin pressure dressings. Multiple blood transfusions were given and he was placed on a diet rich in vitamins. On September 18, 1941, when the patient was first seen by us in consultation a hemolytic *Staphylococcus aureus*, hemolytic streptococcus and a hemolytic *B. coli* were cultured from the bleeding and infected wounds. The following day applications of zinc peroxide suspension were started, and the previously hemorrhagic, dark red infected granulation tissue became healthy appearing and bloodless in less than 48 hours. Within 14 days the granulations had become flat and pinch-grafts were successfully applied September 25, 1941 and October 6, 1941. The application of zinc peroxide was resumed 12 hours after the grafting. Except for a few small granulating areas the wounds were completely epithelized by October 19, 1941, and the zinc peroxide dressings were then discontinued. Straight leg traction and exercises overcame the flexion contractures of his legs.

Except for a short vacation during the holiday season he remained hospitalized until March 15, 1942, at which time the legs were completely epithelized (Fig 2 B).

Discussion In each of these three cases the complication of bleeding was very serious, and always associated with chronic infection, but never with jaundice, low prothrombin time, or other obvious manifestations of liver deficiency. This type of bleeding, developing spontaneously during the granulating stage, is not to be confused with that occurring earlier, either due to depressed blood prothrombin levels^{4, 5} or separation of large infected sloughs. The cause of the bleeding tendency and the explanation of the effectiveness of zinc peroxide are obscure. According to Harkins,⁷ hemorrhage from superficial vessels may occur either during sloughing or later in the granulating stage of burns. There is considerable evidence that some bacterial product produces the bleeding. The constant association of this complication with infection, as noted by Gunn and Hillsman,² and as demonstrated by our cases, supports this view. The continued oozing of blood indicates that the hemorrhage is of the capillary type, which, occasionally, may be the result of damage to the capillaries by bacterial toxins.⁶ Likewise, the rapid arrest of the bleeding, coincident with the control of the infection by zinc peroxide, strongly suggests that its bactericidal and detoxifying action are responsible for its effectiveness.

Although zinc peroxide is usually considered to be indicated in lesions contaminated or infected by anaerobic or micro-aerophilic bacteria, Johnson and Meleney⁷ have demonstrated that this substance also possesses a bactericidal action *in vitro* for hemolytic streptococci and pneumococci, and a detoxifying or destructive action on the hemotoxins of the streptococcus and gas bacillus. As relatively resistant to the action of zinc peroxide they

listed the staphylococcus, *B coli*, *B pyocyaneus*, and *B proteus*. We have been able to show a similar destruction of the hemolysin of the staphylococcus and of the *B coli* as well as the streptococcus after incubation for half an hour with zinc peroxide.

A study of the bacteria isolated from each case shows that the great majority were hemolytic varieties, and that the hemolytic *Staphylococcus aureus* was the only one common to each case (Table I).

TABLE I	
BACTERIA ISOLATED FROM BLEEDING BURNS	
1 R C	Hemolytic <i>Staphylococcus aureus</i> Nonhemolytic <i>Staphylococcus aureus</i> Nonhemolytic anaerobic streptococcus
2 I R	Hemolytic <i>Staphylococcus aureus</i> <i>Streptococcus fecalis</i> Nonhemolytic <i>Staphylococcus albus</i>
3 M L	Hemolytic <i>Staphylococcus aureus</i> Hemolytic streptococcus Hemolytic <i>B coli</i>

Certain strains of the *Staphylococcus aureus* may produce a variety of toxic substances in artificial culture media, including hemolysin, leukocidin, necrotizing toxin, lethal toxin, gastro-enteric toxin, plasma coagulase, and fibrinolysin. We have found no reference to the ability of staphylococcal toxins to cause hemorrhage, in fact, plasma coagulase supposedly favors septic thrombosis in staphylococcal infections. It is possible that this organism produces an additional toxic factor which is responsible for this type of bleeding.

Attempts to produce capillary hemorrhage from granulating surfaces of burns in dogs by the injection or continuous application of bacterial free filtrates rich in staphylococcal, streptococcal, and *B coli* hemolysins have failed.

SUMMARY Three cases of chronically infected burns are presented in which a late and serious complication was continuous capillary bleeding. After many types of local therapy had failed, the application of zinc peroxide immediately stopped the bleeding. If the zinc peroxide was discontinued, the bleeding recurred within a few days. Reapplication of the zinc peroxide again quickly controlled it. The nature of the bleeding and the action of the zinc peroxide remain unexplained.

CONCLUSIONS

In conclusion we wish to emphasize the following points in the management of these and similar cases:

- (1) The prevention of this or other types of infection by careful debridement and cleansing of the freshly burned area.
- (2) The advantage of careful bacteriologic cultures.
- (3) The effectiveness of zinc peroxide dressings in the control of this type of bleeding as well as of the infection.
- (4) The prevention of contractures.

- (5) Adequate blood transfusion to restore the red blood corpuscles and hemoglobin to normal levels
- (6) Skin grafting as early as possible
- (7) Reapplication of zinc peroxide within 12 hours after grafting

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DISCUSSION—DR FRANK L MELENEY (New York) I wish to say just a few words about Doctor Altemeier's paper which interested me a great deal. We have had similar experiences in bleeding from chronically infected wounds when using zinc peroxide with cessation of bleeding, but they were not quite so dramatic as the cases which he has presented.

It will be remembered that the chronic, undermining, burrowing type of ulcer, in which the value of zinc peroxide was first demonstrated, previous to that demonstration was very frequently associated with a profuse hemorrhage, and even fatal hemorrhage when there was erosion of some large blood vessel. Further than that however, in some of the chronic cases one of which Dr Sumner Koch will remember even without serious bleeding there was frequently a very rapidly developing anemia which could only be controlled by transfusions. However with the use of zinc peroxide in that particular case the first result was the rise in hemoglobin and red cells, and the end of the necessity of transfusion, so that besides the immediate action on the surface blood vessels and on the deep blood vessels there is another hemolytic action which is probably generally absorbed into the blood stream and acts upon the blood-forming organ.

I believe that these cases represent secondary hemorrhage, similar to that which we have all seen in our experience from continuous severe infection.

As Doctor Altemeier has said, we demonstrated the effect of zinc peroxide on the growth organisms *in vitro* and we found that the action was most striking upon those which were most highly anaerobic but the action was also present, at least bacteriostatic if not bactericidal on the micro-aerophilic organisms and certain of the aerobic organisms.

The experiments were done first with very high dilutions of zinc peroxide (half of 1 per cent) which showed the lethal action on anaerobic or micro-aerophilic organisms and required 1 per cent 5 per cent and even to 20 per cent to be bacteriostatic on the aerobes. That was demonstrated on the hemolytic *Staphylococcus aureus*. I think that Doctor Altemeier, if he still has those cultures might attempt to demonstrate the bacteriostatic action upon the organisms which were found in these cases, not only in pure culture but in mixed culture because it is known that organisms in skin biopsies will often have an action which they cannot produce in pure culture.

DR WILLIAM A ALTEMEIER (closing) I want simply to mention that we have seen two additional cases of burns which have had this bleeding tendency, but which were lesser in degree and which of course we have not included in the report.

Doctor Meleney has asked me to state that there are eight units that have been set up throughout the country under the auspices of the National Research Council for the study of contaminated wounds and burns and that during the coming year we hope to answer many of these problems that have been discussed.

A SIMPLE METHOD FOR ESTIMATING PLASMA PROTEIN DEFICIT AFTER SEVERE BURNS *

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THOUGH the importance of plasma transfusions in the treatment of burn shock is now generally accepted, there is less agreement in regard to the amount of plasma to be given, and the timing of its administration. Increasing experience indicates that it is difficult to set up a "rule-of-thumb" which will cover even a majority of the requirements of all patients, and that plasma dosage is an individual problem which varies with each patient.

That there is a need for a simple and accurate method for determining plasma loss caused by burns is evidenced by the many methods which already have been suggested^{1, 2, 3, 4, 5}. The formula offered by the authors in a previous contribution¹ meets one of these requirements, namely, accuracy, but it lacks the virtue of simplicity. Further experience has shown that to be practical for general use such a formula should require but a minimum of laboratory data and mathematical calculations. We, therefore, offer as a key to the use of our formula a chart from which the plasma protein deficit may be read directly if the hematocrit or hemoglobin level, plasma protein level, and body weight are known.

This paper will present the chart, describe its use and also give a derivation of the authors' equations for calculating plasma protein deficits resulting from severe burns.

A CHART OF PROTEIN DEFICITS AFTER BURNS

In order to simplify the calculation of protein losses resulting from severe burns values were calculated from the authors' equation¹ for the average adult with a normal hematocrit of 45 per cent cells, and a body weight of 70 Kg (154 lb). The calculated protein deficit, in grams, was plotted against the assumed hematocrit values for several plasma protein levels as shown in Chart I. Hematocrit values are represented by points on the horizontal base line, plasma protein deficits or equivalent plasma volumes by points on the vertical margins, and plasma protein concentrations by the curves. Therefore, each vertical line in the chart represents a given hematocrit value and each horizontal line a plasma deficit. To read the deficit for a burned patient, take the point where the vertical line corresponding to the observed hematocrit value intersects the curve corresponding to the estimated plasma protein level, interpolating whenever necessary. The horizontal line

* Read before the New York Surgical Society, New York, N Y, March 11, 1942

from this point to the left margin of the chart indicates the plasma protein deficit, in grams and to the right the equivalent volume of normal plasma. If the weight of the patient differs markedly from 70 Kg., for which the calculations were made, the deficit read from the chart must be multiplied by a suitable factor. An example is given on the chart. If only the hematocrit can be determined the protein level is assumed as 60 to 70 Gm/100 cc during the first 48 hours following the burn, provided the total intake of fluids is restricted to three liters per day. It should be pointed out that large errors may be introduced if the protein level is unknown. In the uncontrolled burn case the protein level may vary between wide limits.

Hemoglobin levels equivalent to each hematocrit value may be substituted on the horizontal axis. This can be done because the chart defines the relationship of hemoconcentration to plasma protein loss caused by severe burns. The limitations of this procedure will be discussed below.

The chart cannot be used directly for burned cases complicated by hemorrhage, anemia or polycythemia. The anemic individual, especially a child, presents a problem not easily handled by any chart or fixed rules. A whole series of charts, one for each basal hematocrit, is needed for the entire range of anemias. The chart may be used if due allowances are made for the degree of anemia. At the same hematocrit level the plasma deficit for an anemic individual is 20 to 100 per cent greater than that for a person with a normal hematocrit. Therefore, values from the chart are minimal and must be increased proportionally for the anemic patient. This is also true for the burned patient who has lost red cells by hemorrhage. In the patient with polycythemia the protein deficit is considerably less than the value indicated by the chart. Allowances must be made for added red cells if a whole-blood transfusion is given. In all of these instances the most dependable value for the protein deficit is obtained by substituting probable normals in the formula derived below and calculating.

DERIVATION OF THE EQUATIONS

The calculation of plasma volume changes and protein deficits is based on several assumptions which do not meet the rigid requirements for laboratory research data but are sufficiently valid for clinical use. Normal plasma volume, in liters, is taken as 5 per cent of the body weight in kilograms ($0.05 \times W$). Normal plasma protein level is assumed to be 70 Gm per 100 cc. Hence, total circulating plasma protein is $0.05 \times W \times 70 \times 10 = 3.5W$. The change in plasma volume for a unit indicated by changes in serial hematocrit values may be taken as representative of the entire plasma volume. It is further assumed that the total volume of cells in the vascular tree does not change significantly during a series of observations considered here. The equations cannot apply if there has been any marked change in red cell volume through hemorrhage, either external or internal, transfusions of whole blood or osmotic shifts of water. If the cell volume under normal conditions = H_n per cent by volume of whole blood, then $100 - H_n = cc$

plasma per 100 cc whole blood. Also, unit volume of plasma per unit volume of cells will be

$$\frac{\text{Plasma}}{\text{Cells}} = \frac{100 - H_n}{H_n}$$

In like manner, when the plasma volume is suddenly changed by extravasation of plasma (or by dilution) without appreciable change in cell volume, the new cell volume is designated as H_o per cent by volume of cells in whole-blood, and $100 - H_o = \text{cc plasma per 100 cc whole-blood}$. The plasma volume per unit volume of cells is

$$\frac{\text{Plasma}}{\text{Cells}} = \frac{100 - H_o}{H_o}$$

Since unit cell volume is the same in both instances the ratio of the second plasma volume to the normal volume may be written

$$\frac{\frac{100 - H_o}{H_o}}{\frac{100 - H_n}{H_n}} = \frac{(100 - H_o)H_n}{(100 - H_n)H_o}$$

This ratio multiplied by the initial plasma volume ($0.05W$) gives the calculated plasma volume at any given value for H_o

Plasma volume at hematocrit

$$H_o = \frac{(100 - H_o)H_n 0.05W}{(100 - H_n)H_o}$$

If the concentration of protein in the altered plasma volume is P_o Gm per 100 cc the total quantity of circulating protein is

$$\frac{(100 - H_o)H_n 0.05W \times P_o \times 10}{(100 - H_n)H_o}$$

The protein deficit is the initial plasma protein less this value or Protein deficit in grams equals

$$3.5W - \frac{W(100 - H_o)H_n P_o}{2(100 - H_n)H_o}$$

The terms may be redefined

W = Body weight in kilograms

H_n = Normal hematocrit, % per cent cells

H_o = Hematocrit, % per cent cells, after the burn

P_o = Plasma protein, Gm / 100 cc, after the burn

In a similar manner accurately determined hemoglobin levels may be used to express plasma loss because there is a remarkable constancy in the size and hemoglobin content of the red cell in normal persons^{6,7}. The content

* The total cell volume rather than the usual hematocrit value gives more accurate results when there is a marked leukocytosis

of hemoglobin in blood is, therefore, proportional to the total volume of red cells or the hematocrit value. Obviously, the volume of plasma is the difference between the total blood volume and the cell volume. The calculation is made in this manner. Let K = Grams hemoglobin in 100 cc packed cells. Let Hb_n = Grams hemoglobin in 100 cc normal blood. Let Hb_o = Grams hemoglobin in 100 cc whole-blood which, through changes in plasma volume only, has more or less hemoglobin than the normal level. Then $K - Hb_n$ is a measure of normal plasma volume, while $K - Hb_o$ is a measure of the altered plasma volume after the burn. From this point the derivation is identical with that of the hematocrit plasma protein equation presented above. The final equation takes the form: Protein deficit in grams equals

$$3.5W - \frac{W(K - Hb_o)Hb_nP_o}{2(K - Hb_n)Hb_o}$$

Key W = Body weight in kilograms
 K = Gm hemoglobin in 100 cc packed cells
 Hb_n = Gm hemoglobin in 100 cc normal blood
 Hb_o = Gm hemoglobin in 100 cc blood after the burn
 P_o = Gm protein/100 cc plasma

This equation, relating plasma volume changes to hemoglobin levels, gives the same calculated deficits shown by Chart 1. The equivalent hemoglobin level is substituted for each hematocrit figure on the horizontal axis. Such equivalents, calculated from Haden's normals, are shown in Table I. Similar equivalents may be calculated for the normals established in any other laboratory.

TABLE I
EQUIVALENTS CALCULATED FROM HADEN'S NORMALS

Hematocrit % Cells	Hemoglobin Gm /100	Hemoglobin % Normal
45.0	15.40	100
47.5	16.25	106
50.0	17.10	111
52.5	17.96	116
55.0	18.82	122
57.5	19.67	128
60.0	20.53	134
62.5	21.40	139
65.0	22.25	144
67.5	23.10	150
70.0	23.98	156
72.5	24.82	161
75.0	25.70	167
77.5	26.54	172
80.0	27.40	178

Two serious difficulties arise in using hemoglobin levels for estimating plasma volume changes. The error in hemoglobin determinations, by the widely used methods, is entirely too large for the present purpose. The gasometric methods are quite accurate but are not suitable for routine use,

but hemoglobin levels, determined as oxyhemoglobin, with an accurately calibrated photoelectric colorimeter, are quite reliable and may be used whenever available. In the second place, a marked leukocytosis (usually seen in severe burns) causes a discrepancy between the total cell volume and the hemoglobin level. This disparity is increased by a swelling of the red cells following a hemorrhage, as observed by Biennan.⁸ For these, and other reasons, the hematocrit is the method of choice in following burned patients.

The above equation represents a general type of expression which may be modified to show a variety of relationships. In a previous publication,⁹ the same mathematical reasoning was used to express the total base changes in extracellular fluid. The validity of this reasoning depends on (1) the accuracy of assumed normal values, (2) the constancy of the total circulating red cell volume, (3) the fidelity with which the total plasma volume changes are reflected by a changing plasma cell ratio in the large vessels. The magnitude of the errors introduced by each of these factors has not been evaluated. In a series of burns, seen at the Pennsylvania Hospital, the calculated protein deficit appeared to be within 20 per cent of the quantity used in restoring the circulation to the assumed normal. This is sufficiently accurate for clinical purposes.

Discussion—A sharp distinction should be made between plasma protein deficit and plasma dosage in severe burns. The magnitude of the protein deficit is only one factor in determining the plasma dosage. Other factors which must be considered are (1) blood volume depletion apart from plasma protein loss, (2) location and depth of burn, as well as area involved, (3) time elapsed after burn, (4) rate of protein leakage from vascular bed, and (5) complicating factors, such as condition of the heart and kidneys, degree of generalized edema and auxiliary medication (cortical hormone). The state of the peripheral circulation is the final criterion for giving plasma transfusions during the first two or three days following the burn. If, on taking all factors into consideration, a given dose of plasma does not produce the expected change in peripheral circulation, additional plasma must be given.

At no time during the course of a burn is it advisable to compensate completely for the plasma protein loss by a single large transfusion, given rapidly. For the first 40 hours plasma continues to leak from the capillaries, and if a large transfusion be given within that time, an appreciable amount of the transfused plasma leaks out.¹ It is the authors' policy to give, during this period, continuous plasma infusion in sufficient quantity to (1) keep the patient out of circulatory failure, and (2) keep the hematocrit down to within 10 points of normal for that particular patient. After the period of excessive plasma leakage the hematocrit and plasma protein are again determined, and the deficit calculated. Then plasma, equivalent to 80 or 100 per cent of the calculated deficit of protein, is given slowly by a continuous drip. A quantity of plasma greater than the calculated deficit would increase the blood volume above the normal. Too rapid an infusion might lead to cardiac embarrassment or to pulmonary edema in a patient with poor reserve. As pointed

out by Harrison and Picken,¹⁰ the last two complications are very real dangers when giving an overdose of plasma

The present tendency for standardizing plasma dosage according to arbitrary rules is mentioned to deplore the practice. It would seem better to fit the plasma dose to the patient rather than to fit the patient to the rule. An arbitrary dose of plasma may be insufficient to correct the circulatory impairment in one patient. The same quantity of plasma may be a huge overdose, which will produce dire consequences in another patient.

CONCLUSION

A simple chart showing the relationship of plasma loss and hemoconcentration in severe burns has been constructed from the authors' equation. The plasma protein deficit in burned patients may be read from this chart when the hematocrit, plasma protein level and body weight are known. Under certain conditions accurately determined hemoglobin levels may be substituted for the hematocrit value.

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RECENT TRENDS IN THE THERAPY OF BURNS*

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FATAL BURNS cause death mainly in three ways. Deaths within the first 48 hours are usually due to shock. Those from the fourth to the seventh day are usually due to changes in the parenchymatous organs and the late deaths are usually due to infection and malnutrition.

The *systemic* treatment of burns has been developed on the basis of the experimental work of such men as Underhill, Blalock, and Harkins, and now appears to provide a sound basis for the treatment of shock. It has not, however, made such convincing progress in the prevention of damage to the parenchymatous viscera. The result, therefore, of improved systemic treatment has been to prevent some deaths but merely to postpone others.

The problem of infection is no longer solely in the domain of local treatment. The sulfonamides have come to occupy an important place in the treatment of burns as they have in the treatment of all other types of open wounds. They are useful systemically as well as locally. Since the advent of the sulfonamides, the local treatment of burns, which was stabilized in 1925 by the advent of tanning, is now in a state of flux. The closed methods represented by applications of tannic acid, silver nitrate, gentian violet, or triple dye are challenged by a variety of open methods including vaselined gauze and compression dressings (Koch and Mason), sulfanilamide powder and vaselined gauze (Colebrook), saline compresses, and sodium hypochlorite irrigations with the aid of oiled silk envelopes (Bunyan and Stannard). Plaster encasements have been used recently with success in England. A compromise method of considerable promise is the sulfadiazine triethanolamine spray devised by Pickrell. This combines the advantages of the local application of sulfadiazine with the formation of a dry semitransparent membrane which is adherent to the burned surface, yet apparently forms without coagulating living tissue.

As shock has been the most important cause of death its treatment will be considered first. It is now generally agreed that a reduction in blood volume is the most constant change in shock and that restoration of the blood volume results in striking clinical improvement. Furthermore, in shock, due to burns, the loss of blood volume is almost entirely a loss of plasma as opposed to cells. For this reason, in burn shock, the hematocrit may be used as a measure of the plasma loss.

The most important developments in the field of shock therapy in burns are

- (1) Recognition that the physiologic requirement of the burned patient is plasma

* Read before the New York Surgical Society, March 11, 1942

- (2) That plasma should be given quantitatively
- (3) That over half the plasma loss may occur within an hour of the burn
- (4) That there is a continued loss of plasma for some time after the burn
- (5) That the rate of loss probably varies with the amount of plasma in the circulation as well as with the severity of the burn

The high hematocrit and hemoglobin concentrations occurring in the blood of burned patients led Underhill to regard dehydration as an important aspect of burn pathology. Fluids were forced by mouth, if the patient was able to drink, and were given parenterally in the form of glucose and saline solutions, if vomiting occurred.

Interestingly enough, excellent evidence of the difficulty of replacing lost plasma with colloid-free solutions was obtained as early as 1920, when Smith and Mendel showed that a rabbit could be given intravenously an amount of saline equal to his entire plasma volume as rapidly as possible and that by five minutes after the infusion over 90 per cent of the fluid would have left the circulation.

More recently, Minot and Blalock have shown that the intravenous administration of colloid-free solutions to animals in shock actually augments the plasma loss, that is, it washes the plasma protein out of the circulation.

The use of whole blood transfusions was undoubtedly an advance, however, as there is little loss of erythrocytes and as the blood of burned patients is already too concentrated, it is illogical to use whole blood if plasma is available. This is particularly true if the plasma is still leaking from the circulation. It should be remembered that the viscosity of the blood increases much more rapidly than the hematocrit, as blood becomes more concentrated. Trusler, Egbert, and Williams have recorded failure to relieve the blood concentration of a severely burned patient by means of whole blood transfusions. Only after resorting to plasma transfusions were they able to bring about clinical improvement in this case.

The special usefulness of plasma in the treatment of burns is now widely accepted. There is, however, much less appreciation of the quantity of plasma commonly lost by patients with burns. There is rather good evidence that the loss of plasma usually amounts to at least 30 per cent before very marked clinical symptoms appear and that in burns of moderate severity it may frequently amount to as much as 40 to 50 per cent. As the total plasma volume of a 154-pound individual is normally 3,500 cc, the loss commonly runs from 1,200 to 1,700 cc. A 500 cc infusion will, therefore, be a step in the right direction but will fall far short of the full requirement of the patient.

An important observation which has been made by various authors is that a marked reduction of the plasma protein concentration commonly develops simultaneously with the rise in the hematocrit so that within an hour or two

after a burn hypoproteinemia appears. This, of course, calls for additional amounts of plasma.

It should be emphasized that it has been the development of the blood bank and the availability of large amounts of pooled plasma which have made quantitative treatment of burn shock with plasma practical.

The plasma loss begins almost at once and a 20 per cent loss has been observed within 15 minutes after a burn in a case treated at the Pennsylvania Hospital. It is essential to have plasma available for immediate infusion in cases of this type. Another important point in the management of burn shock is the question of the duration of the plasma leakage. Investigators do not

*Relation of Plasma Transfusions to
Loss of Plasma Protein from the Circulation.*

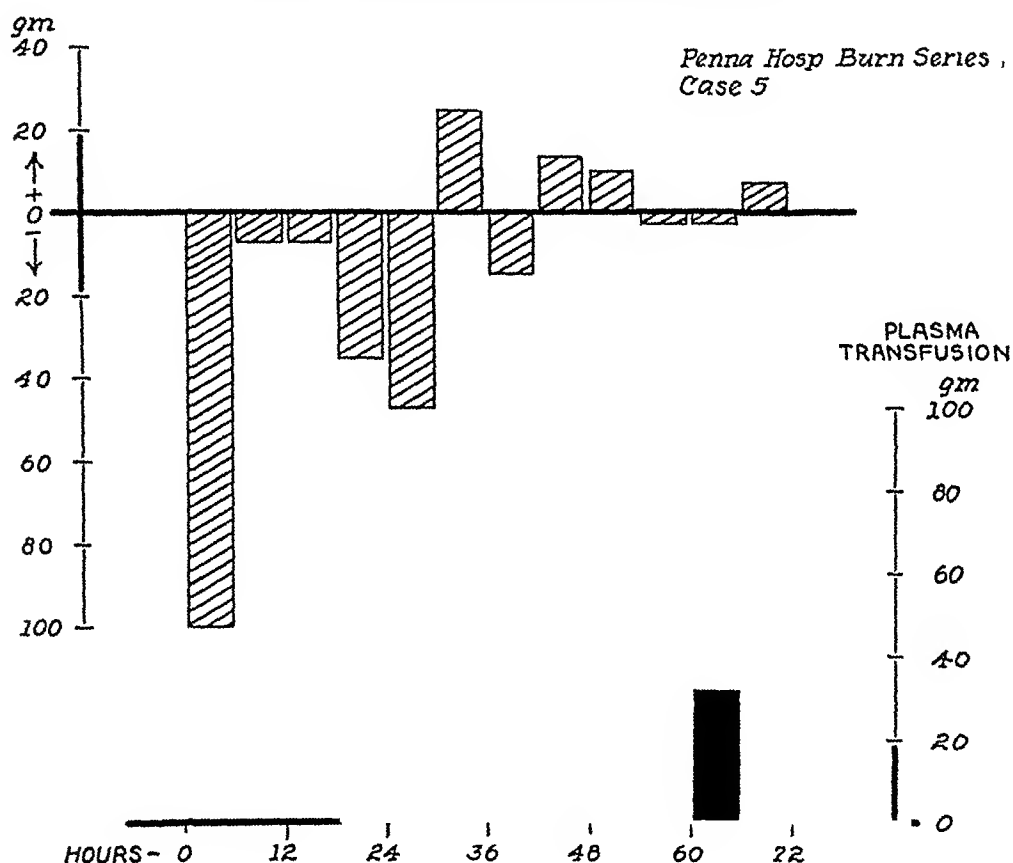


FIG 1

agree on whether this leakage is both local and general, or whether it is purely local, but there is no question that it persists for some time after the burn. The work of Elkinton, Wolff, and Lee gives the plasma volume curves of four patients, and indicates the response of burned patients to large plasma infusions at varying periods after the burn. The infusions given after the fortieth hour were for the most part retained, whereas those given before the fortieth hour were largely lost. Undoubtedly there is some individual variation, but these studies gave the first real indication of the duration of the increased capillary permeability. Furthermore, they indicate another point of some importance, and that is that the addition of large amounts of plasma to what may be termed a leaky circulation leads to a more rapid plasma loss, with the

result that a greater total quantity of plasma is extravasated than would otherwise have been the case. Blood chemical studies on these patients were done at six-hour intervals so that it is possible to estimate the relative amounts of plasma protein in the circulation at the end of each six-hour period and by knowing how much plasma the patient received during the period, it is possible to calculate how many grams of protein were lost each six hours. Figures 1 and 2 show the result of such a study. In the first, a large infusion was followed by a large increase in the plasma loss. In the second, as long as the plasma was given in small quantities, relatively little loss occurred (Case 9). Therefore, until a satisfactory method is found for restoring capillary permeability to normal promptly, it seems better to administer the plasma

*Relation of Plasma Transfusion to
Loss of Plasma Protein from the Circulation*

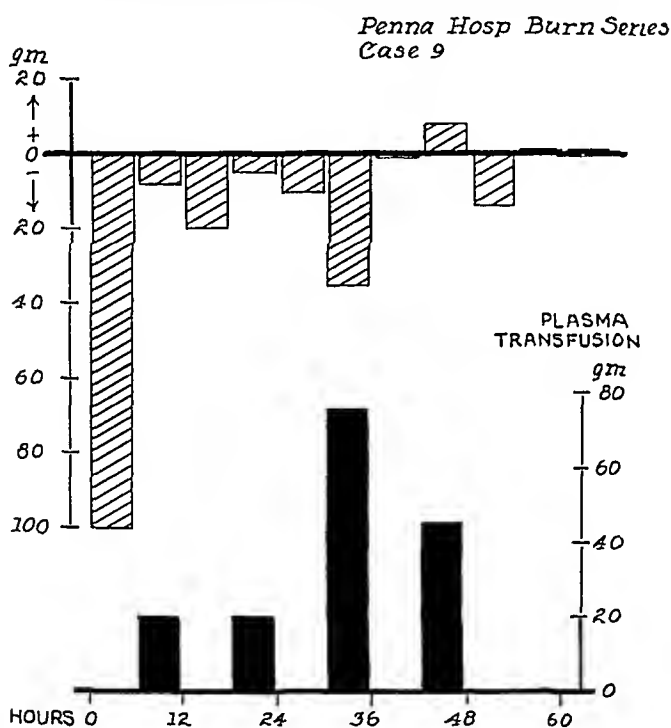


FIG 2

gradually by continuous intravenous drip, rather than to give large infusions rapidly before the capillary permeability has had time to recover.

Several other measures have been recommended for treatment of burn shock. Morphine remains generally accepted. The head-down position is often of value as a temporary measure. The use of oxygen has been endorsed by Schnedorf and Orr, and its usefulness in severe shock questioned by H. A. Davis. As the anoxia of burns is a stagnant anoxia and not due to any lack of oxygen in the alveoli, it is unlikely that oxygen will be of very dramatic value in burn shock, though it must add something to the saturation of the arterial blood. The value of external heat has been investigated, and experi-

mental evidence by Blalock and Mason, shows that excessive external heat hastens the deterioration of animals in shock. It is thought that this is due to the opening up of peripheral vessels with a resultant diminution in the availability of blood for vital centers. Temperatures up to 85° F are probably safe and clinical experience indicates that they are desirable.

In the field of *local* treatment, developments have been many and recommendations numerous. Many of the new forms of treatment are, of course, mere elaborations of earlier methods. Out of much that is controversial, two important trends are discernible: first, a distrust of the tannic acid treatment, and, second, an increasing use of sulfonamides. In both these trends the British have been leaders. Tannic acid is considered by Wakeley to have



FIG 3

FIG 4

FIGS 3 and 4—Picture October 23, 1941, showing distribution of burn. Sulfonamide powder is conspicuous.

given bad results in burns of hands and face. Wakeley presented roentgenograms of hands showing sterile necrosis of the distal phalanges attributed to the constricting effect of the eschar on the circulation. In facial burns instances of ectropion with corneal ulceration were also reported. While the British are not unanimous on this point, such a large majority feel that the stronger tanning agents should not be used on hands and face that they have been largely given up in this Country for these areas. It would seem that the sulfonamide preparations are among the most promising substitutes.

The use of sulfanilamide in the local treatment of infected burns was begun by Leonard Colebrook on a series of 32 men evacuated from Dunkirk. In our experience, it has been the most efficient agent for clearing up infected burns so far available.

The same method has been used many times in the treatment of fresh burns. The most extensive burn in which we have used this method is shown in Figures 3 and 4. In this case sulfathiazole was employed (Rufus Dixon).

The sulfonamides are being prepared in a number of different vehicles. Straight lanolin or vaseline bases are unsuitable because sulfonamides are not oil soluble. Jelly bases, such as tragacanth, which contain water, are satisfactory, though this material may not be available because it has come from the Far East. Emulsions of oil droplets in water are fairly satisfactory bases, such as aquaphor, while emulsions of water droplets in oil are not recommended. Pickrell has developed a new type of base during the past two years at Johns Hopkins. His preparation consists of a 3 per cent solution of sulfadiazine in an 8 per cent aqueous solution of triethanolamine. This solution is sprayed on the burn after debridement and dried. After repeated and frequent sprayings a thin transparent film forms over the burned surface which becomes dry. Excellent results have been obtained with this method. Its chief drawback is that it takes considerable time to obtain a dry film, often nearly 24 hours.

With the use of any of the sulfonamides on a large burn considerable absorption takes place. The amount of the absorption is dependent to a degree on the solubility of the drug, so that higher blood levels are apt to be obtained with sulfanilamide than with sulfathiazole. Hooker and Lam have reported levels as high as 33 mg per cent following the local use of sulfanilamide. Nevertheless, sulfanilamide reaches much higher concentrations on the burned surface than do any of the other drugs. In these concentrations it is active against staphylococci and as it is perhaps the least dangerous of the sulfonamides, many persons regard it as the drug of choice for local application. The fact that it can be crystallized in granules, like sugar, prevents the caking which sometimes occurs with sulfathiazole powder. The sodium salts of sulfathiazole and sulfadiazine are soluble, but they are too alkaline for local application.

If Pickrell's method is used, the dry film becomes impermeable so that absorption of the drug ceases within one or two days. Sulfadiazine may be supplied to the area by way of the blood stream after this time by giving the drug orally in doses of 4 to 6 Gm per day.

If sulfathiazole or sulfadiazine therapy is used it is most important to maintain a urine output of at least 1000 cc. If this is not achieved the drug should be stopped or at least used with great caution.

A number of men have recommended the routine use of sulfonamides by mouth after all important burns. The possibility of toxic hepatitis should be kept in the mind because liver damage occurs after most serious burns and it is conceivable that such damage would predispose to liver damage due to sulfonamides. Apparently, this does not occur with much frequency among young individuals but caution should be employed in patients who are aged, and probably in chronic alcoholics as well. Toxic hepatitis rarely if ever occurs following the administration of sulfadiazine.

Davidson originally maintained that one of the advantages of the tannic acid method was that it stopped the local loss of plasma from the burned surface. Numerous studies have shown that the major portion of the lost plasma goes into the tissues and is evident clinically in the form of edema under and about the burn, nevertheless the bleb fluid in second-degree burns often contains 5 to 6 per cent of protein and is probably very similar to plasma. There is no question but that burns treated by open methods, such as sulfanilamide powder and vaselined gauze, continue to weep large amounts of fluid so that the dressings are often saturated each day. If ample plasma is available this may not be a serious disadvantage, but wherever a large number of burns occur together and the available plasma is limited in amount, a method that rapidly tans the weeping areas may permit the saving of more plasma and hence of more lives than the open methods.

Of the other methods of local treatment little can be said. A return to the use of the bath-tub supplemented by careful cleansing and compression dressings has given excellent results in the hands of Koch, in Chicago. Some of the British writers advocate the use of saline compresses alone. The most radical development in bath treatments is the Bunyan Stannard envelope. This is a waterproof oiled silk envelope, made in various shapes so as to loosely encase a limb or a zone of the trunk. The end, or ends, of the bag are cemented to the skin and the space between the skin and the bag filled with saline or weak sodium hypochlorite solution, and irrigated. In some instances continuous irrigations have been carried out and in others irrigations have been used at intervals and the bag inflated with air or oxygen between times. Dilute sulfonamide solutions can also be employed in this way. These envelopes have the great advantage over the old continuous tub treatment, in that they segregate the burned area from other contaminated parts of the body. The mechanical difficulties of keeping the seals waterproof are obvious.

Triple dye preparations have been used extensively both in this country and abroad. They apparently occupy an intermediate position between the stronger tanning agents, tannic acid and silver nitrate, and the sulfonamides and are considered less destructive to tissue than the former but more destructive than the latter. Triple dye does produce an eschar but it forms more slowly than with 10 per cent tannic acid or 10 per cent silver nitrate.

The effect of both local and general measures on the *toxemia* of burns is still a matter of conjecture. It is known that liver necrosis and many of the other changes may be produced merely by shock due to blood loss. Under these circumstances the necrosis is attributed to anoxia and to the fact that the liver cells are very sensitive to oxygen want. However, in a number of the patients studied at the Pennsylvania Hospital, liver function tests gave evidence of severe liver damage, even in patients who were never severely shocked clinically. All patients in which these tests were carried out gave some evidence of the impairment of liver function.

This, coupled with the observation that the changes in liver function begin about the time that the edema fluid is being reabsorbed from the burned

areas, inclines us toward the belief that the changes are due to absorption of toxic materials

Because the liver apparently suffers so acutely in burn toxemia, treatment has been aimed mainly at preventing liver damage and providing supportive treatment designed to facilitate liver repair. It is obviously important to prevent stagnant anoxia and to give sufficient plasma to maintain the circulation clinically from the earliest possible moment. Glucose should be given parenterally until the patient can retain food, when a high carbohydrate, high protein diet (Ravdin, Vars, and Goldschmidt) should be given in sufficient quantity to cover the basal caloric requirement with a 50 per cent excess. Reasons have been advanced for the administration of vitamin C and of thiamin chloride and a liberal vitamin intake should be assured. The early claim that tanning fixed the toxic materials in the tissues has neither been proved nor disproved. The counter claims that the liver necrosis was due to the absorption of tannic acid has not been confirmed.

The most important new factors in the *late* treatment of burns are undoubtedly the Padgett dermatome and the sulfonamides. Small quantities of sulfanilamide crystals do not prevent grafts from taking and do minimize infection during the interval prior to the first dressing. A burned patient is never really safe from bacterial invasion until epithelization is complete and scar tissue continues to form in granulating areas until an epithelial covering is obtained. With the calibrated thickness graft and a field prepared early with the use of sulfonamides, epithelization can be accomplished earlier and the end results are much less disfiguring than has been the case with pinch grafts.

CONCLUSIONS

In conclusion, we may list the more important recent advances in the treatment of burns

- (1) The selection of plasma transfusions for treatment of burn shock
- (2) A realization of the extent, the rapidity of onset, and the duration of the plasma loss and of the advantage of gradual but quantitative replacement
- (3) The use of sulfonamides in the prevention of infection, especially of sulfanilamide for local application and of sulfadiazine for oral administration
- (4) The development of the dermatome for covering the third-degree areas soon after granulations become visible
- (5) Recognition of the importance of nutrition in maintaining the patient with extensive third-degree burns

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DUTIES OF A SURGEON

"Chirurgion, looke to the wounded, and winde up the slaine, with each a bullet or weight at their heads and feet to make them sinke and give them three gunnes for their funeral Swabber, make cleane the ship Purser, record their names Gunners sponge your ordnance Soldiers scour your pieces Carpenters, about your leakes Boatswaine and the rest, repaire sails and shrouds, and cooke see you observe the morning watch Boy fetch my cellar of bottles Master lay him inboard, loufe for loufe Midshipmen, see the tops and yards well manned with stones, fire pots, and brass bales"

—Capt John Smith, "Seamen's Grammar" (1652)

THE LOCAL TREATMENT OF THERMAL BURNS^{*}

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THE LOCAL TREATMENT of thermal burns is of great importance during wartime. Its correct application depends, however, as much on the correct observation of certain general principles of burn management as on the choice and use of some particular remedy. Local treatment is most effective when scientifically applied.

One of the most important of the principles guiding the use of local therapy is the principle of correlation with general treatment. Pack and Davis (1930) stated in this regard that in burns it is "penny-wise and pound-foolish to consume invaluable time in applying perfect local dressings, while the patient is sinking into irrecoverable shock." The obvious advantage of coordinating the local and general treatments does not imply, however, that all local therapy should be postponed until general measures have been completed. Several years ago patients were treated locally with scant regard for general remedies, now the pendulum has in many instances swung too far the other way. While it may not be wise to radically débride a severely burned patient until shock is controlled, a few early and intelligent applications to the burned surface may not only prevent later infection, but actually diminish the progress of shock and associated fluid loss.

The general treatment of burns (Lam, 1941) includes the control of shock, toxemia and sepsis. The general treatment of burn shock, in turn, involves the use of empiric and symptomatic remedies such as morphine, warmth, and vasospastic drugs, as well as (and probably much more important) the use of plasma (or whole blood), oxygen, and possibly adrenal cortical extract. The control and restoration of fluid loss is undoubtedly the cornerstone of all shock treatment. It is only recently that the work of Lee and his collaborators (Elkinton, Wolff and Rhoads) has put the treatment of burn shock on a quantitative basis. This work of the Pennsylvania Hospital group has established the general treatment of burns as a relatively exact science, just as Davidson (1925) improved the local management.

Aside from the all-important principle of correlation with general treatment, several other rules should guide the local therapy of burns. These include (1) Principle of regional variation (2) Principle of time (3) Principle of closure of the wound.

The principle of regional variation implies that not all portions of the body when burned respond in the same manner to the application of medicaments. A specific example of this is the current wave of prejudice against tanning the face and hands. This feeling is especially prevalent in Great Britain and is even had by those who favor tanning other regions of the body. It is quite probable that tanning is not the best method of local treatment for burns of the face, hands, genitalia, perineum and flexor creases of the body.

* Read before the New York Surgical Society, March 11, 1942

The principle of time implies that what may be an adequate treatment six hours after a burn is not suitable 60 hours following the injury. Contrariwise, the fact that certain treatments are suitable for old burns (*e g*, continuous saline baths) does not imply that they are ideal for acute cases in which shock may be present. This same principle works in other branches of surgery, *e g*, the time limit of closure of a compound fracture or the removal of a ruptured appendix, and is likewise modified by other factors than time alone. Since tannic acid seals over thermal wounds, it seems logical that much the same restrictions on its use should be adopted as for primary suture of traumatic wounds. The general appearance of the burn is an influencing factor as well as the time after the injury, but it would be a good arbitrary rule to adopt never to apply tannic acid without some good reason after the first 24 hours. It is certainly true that in certain cases tannic acid may be used on old granulating wounds, as, for example, bedsores, but these should be selected with caution and the degree of tanning obtained is often a disappointment. In Great Britain there has recently been a discussion concerning the merits of late tanning and retanning of burns. Mitchiner (1940) stated "If sepsis occurred the eschar should be removed at once and the area retanned." Cohen (1940) and Ross and Hulbert (1940) advised late tanning. Heggie and Heggie (1940) treated several infected burn cases by cleansing and retanning, using silver nitrate as the antiseptic. Hamilton Bailey (1938) stated that tannic acid can safely be used up to 72 hours after a burn, but Murless (1940) believed there are no time limits, and he applied tannic acid followed by weak methylene blue or brilliant green solution even on old infected burns. Murless stated that pus formation is not an indication for removal of the coagulum or even for incising it. He believed that the mechanism of the beneficial action is much like that of the Orr treatment of fractures applied by Trueta for infected wounds in Spain. Cohen (1940) and Atkins (1940) arguing from experience gained in the evacuation from Dunkirk, also permitted late tanning. These ideas may have some merit, but seem much like a reversion to the old sophistry of laudable pus.

The principle of closure of the wound will be further discussed under the head of skin grafting. It merely involves the prompt grafting of any granulating surface. An arbitrary rule might be made that grafting should be done whenever a granulating surface resulting from a burn is more than 5 cm in diameter or looks as though it would take more than three additional weeks to heal. Exceptions to this rule should be few. The mistake of grafting too little or too late is far more frequent than the reverse. No conscientious surgeon would think of doing a cholecystectomy if he did not know how to close the abdomen, but many physicians attempt the care of third-degree burns who do not know either how or when to graft. The responsibility of the man who first takes care of a deep burn does not end until the surface is epithelized, that is, until the principle of closure of the wound has been observed.

METHODS OF LOCAL TREATMENT

The local treatment of burns is at present in a state of flux. Those who have felt secure in the use of tanning or other standard therapies are beginning

to feel the impress of the newer sulfonamide methods. Recent international developments have increased both the importance of burns and the necessity for a prompt, even if not final, standardization of treatments for use during the period of emergency. In a recent publication (1942) the author discussed over a hundred local treatments of burns. Local treatment has also been reviewed by Penberthy and Weller (1939), Harkins (1936-1938), and McClure and Harkins (1942). In the present discussion, several of the more important or novel groups of these treatments will be discussed. It is only by a survey of the present methods at hand that guidance in the choice of future therapy can be had. Furthermore, as brought out in the discussion of the principles of regional variation and of time, it is of advantage for the surgeon to have more than one method of local treatment at his disposal to fit the peculiarities of the particular case at hand.

(1) *Tanning agents*—These include tannic acid itself in the form of a spray, jelly, powder, or both, tannic acid-silver nitrate, cutch extract, tea, ink, ferric chloride (Coan, 1935), picric acid, aluminum acetate, acetic acid, and several others. Some of the last named in this list are more properly defined as styptics or astringents than as actual tanning agents. Most of the others are variants of tannic acid alone or in compound form. Tannic acid is a readily soluble, nonnitrogenous, amorphous powder obtained from Aleppo galls. It is only slightly antiseptic and is readily contaminated in solution, but in powder form lasts indefinitely when kept protected from light and moisture. On application to a burn surface it forms a white precipitate with the proteins of the exudation from the weeping epithelium. Tannic acid was used by Davidson (1925) as a means of controlling toxin absorption, but whether this or prevention of fluid loss is its chief action is as yet undecided.

Tannic acid may be combined with various antiseptics such as

- (1) Mercuric chloride 1-2 000 (Mitchner 1938)
- (2) Acriflavine 1-1 000 (Wilson 1934)
- (3) Merthiolate 1-5 000 (Noland 1935), 1-10 000 (Martin 1938)
- (4) Dettol 1-5 (Clark and Cruikshank 1935)
- (5) Salicylic acid 1-1 000 (Fantus and Dyniewicz 1937)
- (6) Hexyl chloro m cresol 1-1 000 (Hartman and McClure 1938)
- (7) Sulfonamide drugs

The use of sulfonamide drugs in combination with tannic acid has considerable promise.

Tanning agents have the advantage of rapid action with minimum subsequent nursing care. Usually a 5 per cent solution is advised, but for war use a more rapid tanning is helpful and for this purpose either a more concentrated solution (20 per cent) or combination with silver nitrate (Bettman method, 1935) is suggested. Since the accouterments of the spray technic are best restricted to hospital use, application of a water soluble tannic acid jelly is an advisable first aid remedy. The use of such a jelly will not interfere with subsequent tanning in the hospital and in addition despite its slowness will often have effected an adequate eschar by the time the hospital is reached, obviating the need for subsequent additional tanning.

The importance of repeated painting of the edges of the tanned eschar with various antiseptics has been emphasized in reports of war surgery coming from

Great Britain Butler (1940) advised a water soluble tannic acid jelly, then an 85° to 100° F tannic acid bath for 30 minutes, after which 10 per cent silver nitrate is applied. A heat cradle kept at 85° to 90° F is then put over the patient and the margins are painted three times daily with 1 per cent gentian violet solution. Wallace (1940) painted the edges of his burns daily with gentian violet or acriflavine. Heggie and Heggie (1940) cleansed and retanned several infected cases with good results, especially when the margins were repeatedly painted with antiseptic dyes. In the treatment of war burns Cohen (1940) used 5 per cent tannic acid followed by 10 per cent silver nitrate to produce rapid tanning. For face burns he applied a little petroleum jelly to the eyelids and held cotton wool over them during application to protect the eyes. He reported that burned areas are usually infected from the adjacent skin and that the streptococcus is the commonest type of invader. Brilliant green was found to be particularly effective in preventing such infections, and in his series, he painted the edges of the tan daily with 1 per cent brilliant green in 30 per cent alcohol. This was of special importance for burns of the scalp, forehead and neck. By careful attention to this regimen he was able to keep the scabs on these regions absolutely dry in all cases but two. In his series of 70 cases, 37 were treated by the silver nitrate-tannic acid method with no deaths. The other 33 were treated by either methyl violet or tannic acid before admission, with two deaths, one soon after entrance and one four days later.

The previous application of greasy or oily preparations markedly interferes with subsequent tanning treatment. Benzene, ether, soap, and ether soap (Fantus, 1934) are useful cleansing agents. In wartime, however, most of the burns which are contaminated with grease are received in naval actions and inflammable detergents are not desirable on board ship. To get around this difficulty, the British have used a compound known as red turkey oil.

(2) *Dyes*—The frequent occurrence of streptococci in burns after the first 12 to 24 hours is well known and has been substantiated by the researches of Aldrich (1933) and Clark and Cruickshank (1935). Moorhead went so far as to define a burn as "an infected wound caused by heat." Aldrich introduced the gentian violet treatment in 1933 at the suggestion of Firor to combat this streptococcal infection. The use of gentian violet alone or in combination with acriflavine and brilliant green in the form of the so-called triple or compound dye presents the advantages of antiseptic action and lack of possible destruction of skin islands. On the other hand, its slow action and staining properties render it less useful for combat purposes. However, in combination with silver nitrate it presents practically the same merits as the combination of tannic and silver nitrate.

The triple dye of Aldrich (1937) has the following prescription

R	Crystal violet	Gm	vel	cc
	Neutral acriflavine		45	00
	Brilliant green		22	50
	Water to make		30	00
			3000	00

(3) *Sulfadiazine spray*—As advocated by Pickrell (1941) this is given every hour the first day, every two hours the second day, every three hours the

third day, and every four hours the fourth day. This complicated regimen alone argues against wartime use of the method. In addition, the resultant eschar is so thin that second-degree burns are apt to be painful and transportability of all types is interfered with. This may be the treatment of the future, but at present is not established well enough for general adoption.

(4) *Ointments*—These include those containing sulfanilamide, sulfathiazole, sulfadiazine, or cod liver oil. The author has had most experience with sulfathiazole and cod liver oil, although sulfadiazine may be better. The chief use of these ointments would seem to be on the face, hands, feet, and genitalia. On the extremities, they may be used in the form of pressure dressings.

(5) *Oiled silk (Bunyan) envelopes*—These are chiefly useful in the later stages of burn treatment, although in deep burns of the hands they may be applicable early. The envelopes combine the advantages of the bath method popularized by the Vienna school of dermatologists, Rose of Seattle (1936, 1937), and by Blair and Brown and their associates (1931-1938), as well as of the warm moist air treatment of Smith, Risk and Beck (1939). While the original method described by Bunyan (1941), and used by Hudson (1941) and Hannay (1941), requires irrigation with a special electrolytic solution of sodium hypochlorite, this is not essential and the principle of the envelope is the same when saline or Dakin's solutions are used. It is important that the temperature of the solution be as close as possible to 100° F. Various shaped envelopes can be made to fit different parts of the body requiring treatment. Bunyan reported favorably on use of the method in 200 cases of burns and wounds while Hudson (1941) reported on 27 cases of burns alone. Wakeley (1941) lists the following advantages of the Bunyan envelope method in the treatment of war burns:

- (1) It can be easily and quickly applied.
- (2) The treatment is painless, there are no dressings, and the patients do not lose confidence or become depressed.
- (3) Rapid epithelization takes place and can be seen through the envelope. Skin grafting can be performed at any time after irrigation with saline solution instead of hypochlorites.
- (4) The envelope allows of free movement of the limb without the fear of pain.
- (5) In the difficult cases where fractures exist as well as burns, this method appears to offer a solution. Treatment of ordinary compound fractures has proved successful.

THE IMPORTANCE OF EARLY SKIN GRAFTING

Third-degree burns are by definition those which produce granulating surfaces. As already stated under the discussion of the principle of closure of the wound, early grafting is one of the most neglected fields in burn treatment. A psychologic anxiety should be bred in all surgeons over every extra day that such a wound remains unepithelized. Keloid, contractures, malignancy and increased unsightliness are all more liable to occur with delayed healing.

General care of the patient with control of anemia and hypoproteinemia are essential. Efforts should be made to hasten spontaneous healing, but as Brush and Lam (1942) recently reported, the application of external stimulants of epithelial proliferation are of more psychic than material benefit. Saline soaks and dressings, cod liver oil, acriflavine, oxyquinoline sulphate scarlet R gauze (Bettman, 1931), and sulfonamide drugs all have their place in this phase of the treatment.

Skin grafting itself should depend on small deep (pinch) grafts, thick split (Thiersch) grafts, and dermatome grafts. Of these, the third type is used almost to the exclusion of the other two in the author's practice and will be described more in detail below. Full-thickness and pedical grafts have no place in the early plastic care of burns and should be reserved for subsequent corrective and restorative late plastic care. This latter is done when epithelization is complete.

The technic of taking and applying dermatome grafts can be divided into 12 steps which embody principles laid down by Blair, Brown, Davis, Padgett, Harkins, and their associates, as follows:

(1) *Preoperative Preparation of Granulating Area*—The best immediate preparation is to apply saline dressings for at least 24 hours just before operation. Decision as to the time for grafting depends more on the presence of (a) a healthy pink appearance of granulations, (b) lack of anemia, and (c) lack of hypoproteinemia, than on any bacterial counts or other indirect observations.

(2) *Preparation of Donor Site*—The skin is cleansed with ether followed by alcohol and painted with the special adhesive glue which is allowed to dry for about 60 seconds before taking the graft. The use of ether is important as the glue will not adhere to a greasy surface.

(3) *Anesthesia*—Because of the large surfaces involved and because the grafts are usually sutured in place, gas anesthesia is generally adopted.

(4) *Removal of Grafts*—If the granulating area is the size of the drum surface, one drum of skin is taken. If the desired graft is to be smaller, only part of the drum is coated with the special adhesive glue. If a much larger area is to be covered, several drumfuls of skin are taken and are either applied individually, or better, sutured together in the pattern of the defect to be grafted after the manner of a patch-work quilt according to the method of McPheeters and Nelson (1941). In any case, the adhesive glue is best applied to the drum in a thick layer at one end and smoothed over the drum in as thin a layer as possible using the base of the dermatome stand to distribute the glue. The drum (with the knife set at about 0.6 mm thickness (less for children or those with atrophic skins) is held in the left hand and the knife in the right. Two practical points are to press the upper end of the drum very firmly against the skin where the cutting is to begin, as a good start is essential, and not to allow any assistants to retract the skin as this merely pulls it away from the drum and is harmful. Gradually turning the drum with the left hand and cutting backward and forward with the right, a

graft the size of the drum surface and of uniform thickness is quickly obtained in a majority of the cases

(5) *Dressing Donor Site*—Five grams of sulfanilamide powder are sprinkled evenly over each area 4 x 7 inches (equal to one drum surface) and this is covered with sterile fine-mesh vaselined gauze followed by dry gauze and a tight adhesive tape dressing



FIG 1—Example of neglected burn. This boy was burned 27 months before this picture was taken and he was never grafted during all of this time. This neglect of the principle of closure of the wound has resulted in a severe condition including bony ankylosis of the right elbow and left temporomandibular joints, ectropion of the right eye with tearing and a web deformity of the neck not shown in this picture. Subsequent plastic care improved this patient markedly but not so much as it would have, if applied earlier. (From Harkins H N. The Treatment of Burns, Springfield, Ill., Charles C Thomas, 1942.)

(6) *Transfer of Grafts*—This should be done aseptically when more than one graft is to be taken. During the transfer, the graft should be kept moist with warm (not hot) normal saline solution.

(7) *Preparation of the Granulating Surface*—Granulations are seldom shaved off a burn granulating surface that is less than three months old. Since the ideal of treatment is never to let such a surface go as long as three months, it might be said that to have to shave off granulations means previous neglect. The skin around the surface may be covered with any antiseptic, but the

granulations themselves should be gently cleansed with ether alone. If they are at all infected, sulfanilamide powder (not sulfathiazole, as it tends to act as a foreign body) may be dusted very evenly over the granulating surface. This should be done in a dosage of 1 Gm per ten square inches and it is essential that the coating be more homogeneous than that over the donor site. The grafts are then applied epidermal surface upwards on the sulfanilamide layer, or if this drug was not deemed necessary, directly on the granulations themselves.



FIG 2—Example of neglected burn. This girl, age 18, was burned 14 years previously at the age of four. She was never grafted and ulcers of the upper right thigh are still present.

(8) *Suturing of Grafts*—All dermatome grafts should be sutured in place with fine non-absorbable material. A circumferential ring of continuous suture interspersed with several double-locks or interrupted stitches is advisable for the periphery of the graft. The edge should just overlap the surrounding live skin, while an excess of graft merely dies and invites infection. The graft should be applied with the tension and size as near as possible like that which it had before being removed from the donor area. The bed of the

graft may be sutured through the granulations to the fascia beneath with numerous interrupted stitches or criss-crossing continuous ones. These latter are especially useful when the graft covers a convex surface, as the thread between the stitches holds the graft in place. If enough sutures are placed, very few fenestrations need be made in the graft, as the needle holes permit escape of blood or exudation.

(9) *Dressing Grafted Area*—The importance of this step is shown by the following quotation from Brown, Blair, and Byars (1935): "The dressing fixation is considered a part of the operation and upward of 30 minutes may be required to apply it correctly in extensive cases." The use of a wet dressing is useful in infected cases. In any instance the graft is covered with fine mesh vaselined or xeroform gauze (a little sulfanilamide may be sprinkled on first) and this is covered with a generous layer of cotton mechanic's waste (Mechanic's waste is easier to handle and cheaper than sea sponges, costing only 12 cents a pound). The waste should be autoclaved before use, and gives a very uniform pressure. The dressing should next be anchored with elastic adhesive to the surrounding skin and if possible a splint or encasement applied. Too much pressure is almost worse than too little and should be avoided, but adequate immobilization should be maintained for several days. The fate of a skin graft is sealed during the first 48 hours. In cases with marked infection at the time of grafting an optional method is to incorporate perforated Dakin's tubes in the dressing. Twice daily irrigations with two quarts of saline solution (or tap-water) followed by the instillation of two ounces of sulfadiazine solution seem to be effective in controlling infection. External irrigation by constant drip as described by Harkins (1942) accomplishes the same purpose.

(10) *Changing the Dressing of the Donor Site*—If no infection, as determined by odor, or hemorrhage results, the dressing should ideally be left intact until the area is healed. In many cases, however, the outer dressing should be exchanged for a dry fresh one during the first day or so, but the vaselined gauze should not be removed as long as it adheres (usually 12 to 14 days).

(11) *Changing the Dressing of the Recipient Site*—This should be done at any time from three to eight days following the operation, depending on the amount of infection that is present. When the change is decided upon, it is best to soak the area for some hours beforehand so as to prevent sticking and pulling off of the grafts. Since the donor site must be kept dry, complete tub immersion is not feasible and some type of irrigation or drip is advised. Thus, if the dressing is to be changed in the afternoon, the nurse is instructed to start the drip in the morning. When the time comes for the change, the danger of pulling the grafts off with the dressing is minimal. Irrigation through Dakin's tubes incorporated in the dressing accomplishes the same thing. The stitches may be removed in part at the first dressing although any adherent sutures should be left until at least the seventh postoperative day. Subsequent dressings do not need pressure but can utilize vaselined gauze, sulfanilamide powder, and moist gauze or irrigations with advantage.

(12) *After-Care*—Once the dressing of the recipient site has been changed,

renewals at about 48-hour intervals are necessary until the skin has become firmly established, at which time the bandage may be removed entirely

When the surface is epithelized and the principle of closure of the wound has been fulfilled—then and only then—the responsibility of the surgeon originally caring for the burn ends

COMMENT

For wartime use, simplicity and rapidity of action are essentials of burn treatment. The ideal treatment would probably be the best under all circumstances, but at present it is possible that the methods of burn treatment most suitable in the leisurely course of peacetime practice are not necessarily best fitted to the urgency of war. A rapid tanning of the broad surfaces of the body seems best fitted to the latter



FIG 3—Simple type of external drip used in local care of burn or skin grafts. (From Harkins, H. N. *The Treatment of Burns*, Springfield, Ill., Charles C. Thomas, 1942.)

Since it is extremely difficult to determine the exact depth of injury until late in the course of a burn, even when viewed by experts under the best of conditions, there is little use in recommending wartime determination of burn depth in deciding upon burn treatment. On the other hand, the site of the burn is of considerable significance in this regard. Tanning methods seem less well suited to the face, hands, feet and perineum than do certain of the ointments.

Several problems and details of technic arise which are listed below without comment.

- (1) What is the longest possible interval after a burn that tanning therapy can be applied under optimum conditions?
- (2) What percentage of plasma loss does tanning prevent?
- (3) Assuming that the main purpose of the tanning method is to conserve plasma, if plenty of plasma is available, is tanning still advisable?
- (4) Is tannic acid toxic?

SUMMARY

- (1) Local treatment should be carefully correlated with general treatment
- (2) Rapid tanning of the large flat surfaces of the trunk or proximal extremities seems the best local treatment for wartime use Preliminary first aid use of the slower acting tannic acid jelly may be time-saving in the long run when hospital facilities are not available
- (3) Individualization of burn therapy according to the site of injury is of importance The face, hands, feet and genitalia should be given separate treatment, such as sulfathiazole or sulfadiazine ointment
- (4) Early skin grafting is of prime importance in all third-degree burns

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THE PROCUREMENT AND USE OF BLOOD SUBSTITUTES IN THE ARMY*

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THE RESEARCHES that have been conducted to find an effective means of replacing depleted circulating blood volume in traumatic shock have provided one of the most intriguing chapters in modern medicine. The developments in the field of transfusion therapy in recent years have had a marked influence on the practice of civilian and military surgery.

The contributions of Crile,¹ Robertson,² Cannon,³ and Keith⁴ preceding and during World War I firmly established the use of the blood transfusion as a safe and effective measure. The continued use of whole blood transfusions in civilian hospitals and fixed medical installations in the Army is assured. However, the limitations of whole blood and the difficulty of obtaining it immediately when needed have stimulated a persistent search for other fluids which might be equally as effective and more readily available than blood in the treatment of surgical emergencies. The desire to provide an adequate blood substitute is reflected in the researches on gelatin and acacia carried out by Hogan,⁵ and Bayliss,⁶ respectively, during World War I.

The realization of the need for effective replacement fluids other than whole blood was revived in 1936 by Elliott⁷ when he proposed the use of untyped plasma for the treatment of obstetrical and surgical shock. Renewed impetus was given to this subject with the beginning in 1938 of hostilities in Europe. This unprovoked conquest forcefully brought to the attention of our Army and Navy the necessity of preparing for any eventuality.

In May, 1940, the National Research Council was asked by the Surgeons General of the Army and Navy to act in an advisory capacity on the many medical problems that might arise in the eventuality of active conflict. As a result of this request, a Committee on Blood Transfusions and a Subcommittee on Blood Substitutes were appointed to study the problems confronting the armed services in selecting and procuring adequate quantities of suitable blood substitutes and blood derivatives.

The clinical and experimental work of Elliott,⁸ Strumia,⁹ Mahoney,¹⁰ and Levinson,¹¹ to mention only a few, fortuitously done between 1936 and 1940 strongly suggested the possibility of using blood plasma and serum, and thus paved the way for the adoption of these agents as adequate replacement fluids for the treatment of shock, burns and the emergency treatment of hemorrhage.

As a result of investigations on blood procurement, preservation and transportation of whole blood,¹² methods of preparation of dried plasma and serum,¹³ and the commercial facilities for producing plasma in large quantities, it was concluded by the Subcommittee on Blood Substitutes that dried plasma

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was the blood derivative of choice for the Armed Services. Dried plasma was chosen because of its long preservation period, stability at extremes of temperature, its effectiveness as a replacement fluid and the safety with which it can be administered. It was also agreed that freezing and maintaining this fluid in the frozen state is an adequate method of storing plasma.¹⁴ Plasma preserved in this manner can either be dried from the frozen state or thawed rapidly and injected as wet plasma.

The effectiveness of plasma as a replacement fluid for military use is directly proportional to its availability under combat conditions.¹⁵ In order to make plasma accessible to medical units in the field it is necessary to package

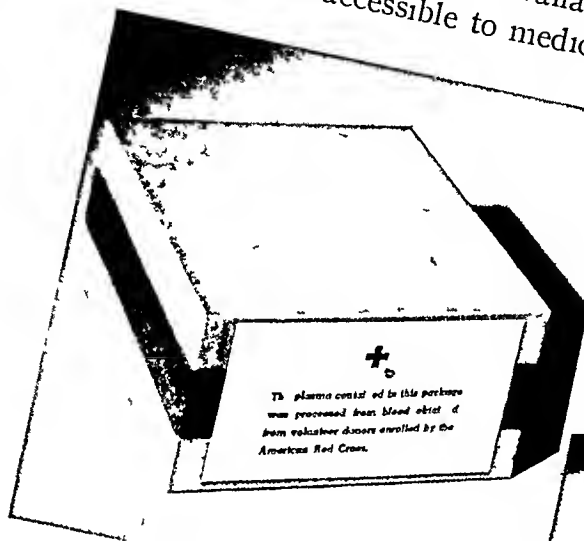


FIG 1—The standard Army Navy package of dried human plasma



FIG 2—Cans being removed from package with draw cord

it with needles and intravenous equipment so it can be regenerated and administered immediately wherever it is needed. A package for this purpose has been developed by representatives of the Army and Navy¹⁶ in conjunction with committees of the National Research Council and this unit is now designated as the Standard Army-Navy package of dried human plasma. The dried plasma, distilled water for reconstituting the plasma, and intravenous equipment are packed together in cans so that the set may be preserved for a period of five years.

A description of this package follows.

The completed package (Fig 3) consists of two 400 cc bottles, stoppered with sleeve-type rubber stoppers and an intravenous assembly in sealed metal cans, packaged in a tape-sealed, water-proofed, fiber-board box. On one end of the box is a label of the biologic laboratory processing the plasma and on the other end is a Red Cross label showing that the blood from which this plasma was made was furnished by volunteer Red Cross donors (Fig 1). The box is easily opened by tearing the tape transversely and ripping it off. The cans fit in the box snugly so a draw cord is provided to facilitate removal of the cans (Fig 2). Also present in the fiber board box is a questionnaire to be filled out by the operator each time a unit is used. When these forms

are filled out properly and sent in for filing, it is possible to compile valuable statistical data on the use of plasma

Keys, spot-welded to the top of each can, are provided for opening them. The can, containing the dried plasma bottle, has packed with it intravenous and double-ended needles and a metal clamp. The plasma bottle and can are sealed under a 25-inch vacuum to keep out moisture. As an added precaution, a bag of silica-gel is placed in the can to adsorb any moisture that may be present. A cloth-tape bail attached to the bottle makes it possible to suspend the container while administering the plasma.



FIG 3—Contents of plasma package

The bottle containing the distilled water, together with the airway assembly and intravenous set, is sealed in another can which is filled with nitrogen. This inert gas is added to preserve the rubber by reducing oxidation to a minimum. The intravenous equipment consists of an intravenous set and an airway assembly. The airway assembly is made of nine inches of rubber tubing with a needle attached on one end for insertion into the rubber stopper and a cotton filter on the other end. The intravenous set consists of 48 inches of rubber tubing which contains a glass cloth filter for filtering the plasma as it is administered. At one end of the tube is an intravenous needle attached to a glass observation tube and at the other a short needle which connects the set to the plasma bottle.

The instructions for the preparation and use of this material are lithographed on the can containing the dried plasma.

The plasma is made ready for use by inserting the double-ended needle, provided for this purpose, through the stopper of the bottle containing the

distilled water (Fig 4) The water bottle is inverted and the other end of the needle is plunged into the stopper of the dried plasma bottle, the negative pressure in this container causes the water to flow in and the plasma goes into solution in about two minutes In order to allow air displacement in the water bottle and speed up regeneration, the needle of the airway should be inserted into the stopper of the water bottle When the water has been transferred the double-ended needle is withdrawn from the plasma bottle The airway and intravenous set are then connected to the plasma bottle and the plasma is ready to be administered (Fig 5)

Based upon the recommendations of the National Research Council, a program was outlined for the collection of blood and the processing and

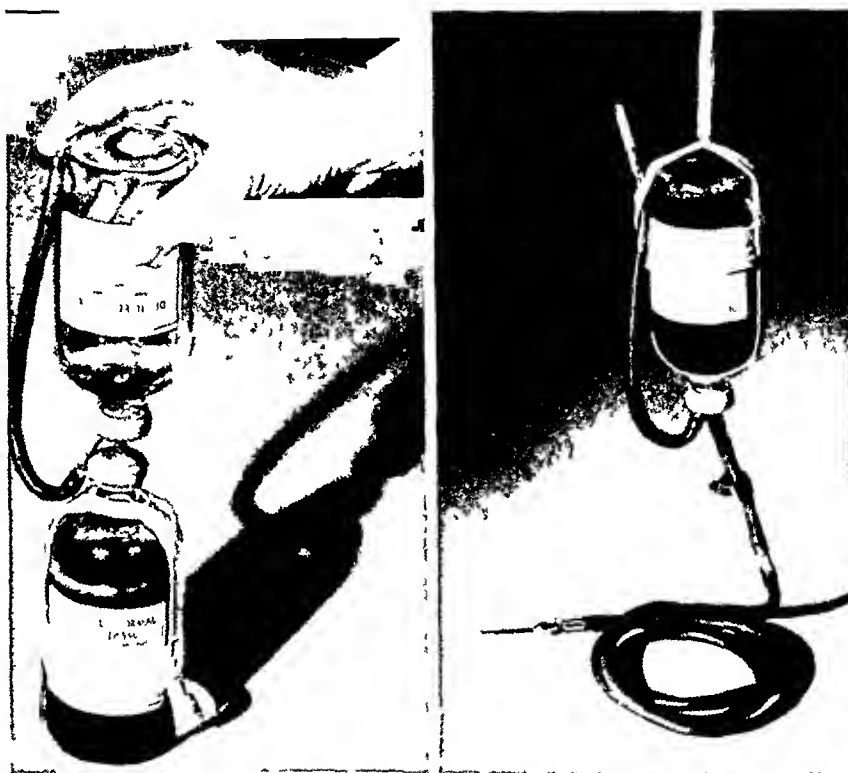


FIG 4—Plasma being constituted with distilled water

FIG 5—Reconstituted plasma ready for administration

drying of plasma The American Red Cross was asked to furnish volunteer donors for this program, the Army acted as the purchasing agent and contracts were made with eight commercial biologic laboratories for the preparation of dried plasma

At the present time, the American Red Cross has 18 bleeding centers operating throughout the country, supplying approximately 15,000 bleedings a week to the processing firms It is anticipated that by July 1, 1942, 350,000 packages of dried plasma will have been delivered to the Army and Navy As rapidly as the dried plasma packages are received at the supply depots they are placed aboard combatant ships of the Navy and are issued to units of the Army going outside the country so that they will be readily available for use Because of the urgent need elsewhere dried plasma is not being issued to medical installations for use in the United States

Approximately 300 reports recording the use of dried plasma in hospitals in this country and at foreign stations have been returned to the Blood Research Laboratory. Two-thirds of these units were administered for the prevention and treatment of shock while the remainder were used in hypoproteinemic states. Definite improvement was observed in all but four cases treated for shock. It is apparent from these reports that when plasma is indicated, it should be started as soon as possible. The earlier plasma is injected after injury, the smaller the amount required to overcome the blood volume loss.

No severe reactions were encountered in this group. One patient developed urticaria, which was localized, and five had chills, but no temperatures above 100°F were recorded.

It is expected that the needs for dried plasma by the armed services will be increased by threefold during the next fiscal year and therefore the program for obtaining donors and preparing plasma is being supplemented with the help of the American Red Cross.

In addition to the national program for the collection and preparation of dried plasma for use by the armed services, the Army maintains a laboratory for the investigation and preparation of blood substitutes and blood derivatives. This Blood Research Laboratory was established in May, 1940, at the Army Medical School, and has operated continuously since that time. In this laboratory, liquid plasma is being prepared from blood collected from volunteer Red Cross donors at the combined Army-Navy Donor Center in Washington. This liquid plasma is being used at Walter Reed General Hospital and shipped unrefrigerated to outlying station hospitals. During the past few months liquid plasma prepared in this laboratory has been preserved by freezing it in a regular ice cream chest. Prior to shipping, the frozen plasma is thawed out rapidly by immersing it in a water bath at 37° C. Plasma thawed in this manner does not contain precipitated protein material. The thawed plasma can be stored at normal room temperature or shipped great distances without refrigeration. This material is arbitrarily given a four-month dating period from the time it is thawed out. Further experience is required to determine how much longer this dating period can be extended. As a result of our experience with liquid plasma, it is conceivable that a dating period of one year might be placed on the thawed wet plasma.

The plasma processing unit at the Naval Medical Center now is supplying thawed wet plasma to all of their medical installations throughout the country. The plasma unit at the Army Medical School is supplying thawed wet plasma to the Army hospitals in the Third Corps Area and is now prepared to supply the First and Second Corps Areas.

During the past 18 months, about 3,000 bottles of liquid and thawed wet plasma have been used locally in the Army and Navy Medical Centers¹⁷ and shipped to service hospitals throughout the United States. Questionnaires have been supplied with these units and approximately 1,500 have been returned for evaluation. Reactions in this group have consisted of localized

urticaria, chills and fever, and, in one case, substernal pain was produced. The reaction rate in this group is 62 per cent. No fatal reactions have occurred.

Properly prepared liquid plasma is stable in the frozen state and may be preserved indefinitely. This method of preservation provides a safe and economical method of making plasma readily available to the military forces in this country. When thawed in the manner described above plasma can be shipped safely in the liquid state unrefrigerated.

Based upon the experience gained during the past 18 months at the Army and Navy plasma centers in Washington, plans have been made by the Army to establish liquid plasma processing centers in each Corps Area to supply all stations in the area, so that every Army hospital will have access to supplies of blood plasma. Plasma made in these centers will be prepared by a standard technic. The medical officers and technicians responsible for running these units will be trained at the Army Medical School and the Army-Navy Donor Center in Washington. This program is under way now and it is expected that within the next few months frozen wet plasma will be generally available to the Army.

Although dried and wet plasma have proved their value as effective replacement fluids in shock and burns, interest in other blood derivatives is constantly increasing. One of the more recent developments, the preparation of human albumin, is worthy of consideration.

Cohn,¹⁸ at Harvard, has been successful in producing human albumin in such form that it can be injected intravenously in the human with relative impunity. Albumin makes up 65 per cent of the plasma proteins and exerts approximately 80 per cent of the osmotic effects provided by the blood plasma. It is stable in the liquid form up to temperatures of 45° C and can be prepared in 25 per cent solution which does not precipitate or become cloudy on standing unrefrigerated for many months.

Human albumin has been accepted by the National Research Council, for the Army and the Navy, as an effective blood derivative for the treatment of shock and burns. It is realized that albumin is not a completely adequate replacement fluid when the patient is dehydrated. In cases of injury complicated by dehydration states it is essential that supplemental fluids and electrolytes be administered by mouth or intravenously when albumin is injected. A word of caution should also be said about the use of albumin in patients where concealed hemorrhage may be a complication. Twenty-five per cent albumin draws fluid into the vascular bed rapidly, thereby raising the blood pressure in a short time. Wounds that are closed while the blood pressure is low may bleed following the injection of albumin, producing massive hematomata. If these occur in the neck, pressure symptoms may result. Therefore, the wounded patient should be observed carefully after albumin is injected to prevent secondary hemorrhage. Great care must be exercised in the use of 25 per cent albumin in casualties with gunshot or stab wounds.

of the chest or abdomen. Where gross hemorrhage is suspected, albumin might best be withheld until the large bleeders can be tied off.

The possibility of providing an effective replacement fluid in a small package has been of tremendous interest to the Army and Navy. Since 100 cc of 25 per cent albumin has an osmotic pull approximately twice that supplied by the Standard Army-Navy package of dried plasma, it is worthy of consideration by the military surgeon for use aboard ship and other places where space is a problem. With this in mind a container, with an intravenous assembly, for packaging and administering albumin has been developed.



FIG 6—Equipment for administering human albumin



FIG 7—Albumin package ready for administration

The package (Fig 6) consists of a 115 cc double-ended vial closed with sleeve-type rubber stoppers. The instructions for preparing the set are baked on the glass vial. A string or cloth tape bail is provided for suspending it. The intravenous assembly consists of a small-bore rubber tube 40 inches long with a connecting needle on one end and a 20-gauge intravenous needle attached to a small glass observation tube on the other. The airway is made of a rubber tube one inch long, containing a cotton filter and a connecting needle. The albumin set may be sealed in a metal can or plastic carton under nitrogen.

The albumin is made ready for use by inserting the connecting needle of the intravenous set through the stopper at one end and the airway needle through the stopper at the other end (Fig 7).

SUMMARY

The program for the collection and use of blood substitutes in the Army has been discussed

A description of the methods of packaging these substitutes to make them suitable for storage and for use wherever necessary has been outlined

The experience thus far gained by the armed services in the use of dried plasma and thawed, wet plasma have shown these methods of storage to be adequate within the limitations outlined in this paper

It is expected that both blood plasma and human albumin will be made available for use by the Army and Navy

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INTRAVENOUS INJECTIONS OF AMINO-ACIDS (HYDROLYZED CASEIN) IN POSTOPERATIVE PATIENTS*

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IN A paper¹ before this Association two years ago, I described clinical experiences with surgical patients who received intravenous injections of a mixture of amino-acids (Amigen†) as a means of supplying protein parenterally. Evidence of its beneficial effects, both clinical and chemical, was obtained. However, the number of cases was small and the occasional occurrence of untoward reactions seemed to demand a larger experience with this new method of intravenous protein alimentation. Accordingly, a large series of injections were made on the wards of the St. Louis City Hospital. We carried out all of the injections ourselves except that when one of us (D O W) entered the Medical Corps of the United States Army, Drs L V Mulligan, T C Tyrell, and W H Elliott substituted for him. All patients receiving Amigen were carefully observed and records kept on a separate form. At least one of us (E B) was present with the patient during all injections in order to make the observations as complete as possible.

TABLE I
SUMMARY OF INTRAVENOUS INJECTIONS OF AMIGEN

Solution Contained				Surgical (Post op) Cases		Medical Cases		Pyrogenic* Reactions	Deaths*
Solution No	Amigen (Per Cent)	Glucose (Per Cent)	Prepared by	Number of Patients	Number of Injections (Liters)	Number of Patients	Number of Injections (Liters)		
1	2.5	10	M J	2	7	49	95	10	5
2	2.5	10	M J	8	17	5	6	1	0
3	2.5	10	B H	42	97	20	39	0	0
4	2.5	5	B H	23	39	21	26	0	2
5	2.5	2.5	M J	66	514	3	6	3	10
6	2.5	2.5	B H	55	100	15	16	1	3
7	5	5	M J	2	36	1	11	0	0
Totals				198	810	114	203	15	20

* No pyrogenic reactions or deaths were due to Amigen (see text)

Procedure—Preparation of Solutions Amigen is an impalpable, nearly white powder which in water forms a clear, amber-colored solution with a pH

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

† The amino-acids used were a mixture (containing also some polypeptides) made by the enzymic hydrolysis of purified casein and prepared and supplied by Mead-Johnson and Company, it is called, and will be referred to as "Amigen"

of 45 Various solutions were used in the present study Their composition is listed in Table I. In general, two methods were used for sterilization The solutions prepared in Barnes Hospital (B H) were passed through a single Berkefeld filter, autoclaved at five pounds pressure for 30 minutes and used soon thereafter The solutions made by Mead-Johnson and Company (M J) were subjected to careful Seitz filtration, but not autoclaved, their sterility was carefully tested before use

As is well known, many febrile reactions with chills are due to the use of distilled water containing pyrogens These pyrogens are products of bacterial growth which may occur even in distilled water which is allowed to stand for any length of time either in a container or in some undrained portion of the apparatus which is not sterile Freshly distilled water coming directly from the condenser of properly designed stills, is not pyrogenic, such water was employed in the preparation of all solutions used in the present study, with one exception The first batch used (Solution No 1) was inadvertently made up with distilled water which was later found to be pyrogenic It is notable that ten of the total of 15 reactions, indeed all which could be explained in no other way, occurred with this solution This defect was, of course, immediately corrected, subsequent solutions were not only made with freshly distilled water, but tested for pyrogens by injection into rabbits

Selection of Cases—No attempt was made to select special cases in this study except that most of them were surgical patients The medical and surgical diagnoses are listed in Table II Nearly all of the patients were dehydrated and ill and needed parenteral fluids, many of them were in a critical

TABLE II
DISTRIBUTION OF CASES

	Number of Patients	Number of Injections
Surgical (postoperative)		
Acute appendicitis mostly with peritonitis	52	201
Intestinal obstruction mostly due to cancer	15	119
Perforated peptic ulcer many with severe peritonitis	12	102
Gastrectomy, mostly for cancer	7	85
Exploratory celiotomy, mostly for cancer	12	57
Herniotomy, mostly ventral	19	67
Fractures	39	65
Cholecystectomy	9	53
Burns	4	10
Miscellaneous	29	51
Totals	198	810
Medical		
Pulmonary tuberculosis	43	56
Senility	24	36
Cardiac disease and hypertension	12	41
Pneumonia	10	19
Alcoholism	3	4
Arthritis	7	12
Miscellaneous	15	35
Totals	114	203
Grand Total	312	1013

condition at the time of injection. They represented, in general, a fairly representative cross-section of the indigent found in a large city hospital.

Rate of Injection—In general, an average rate of 300 to 500 cc per hour (about 5 to 8 cc per minute) was maintained. With solutions containing 2.5 per cent of amino-acids, the amount injected in an hour was, therefore, roughly, 8 to 12 Gm. If this rate were continued for 24 hours, between 200 and 300 Gm of protein nourishment could be thus administered, although the volume (8 to 12 liters) would be excessive. In a few cases the rate was greater, up to 500 and 900 cc per hour of the 2.5 per cent solution. The largest amounts of Amigen were given as 5 per cent solutions (see No. 7, Table I). In two of these patients, 300 Gm of Amigen (with equal amounts of glucose) were injected each day for three days, by means of a continuous venoclysis. Recently, a patient inadvertently received 1,000 cc of 10 per cent Amigen in less than an hour, however, it had been neutralized to a pH of 6.5 by the addition of NaOH. Aside from abdominal pain, nausea, and vomiting there was no untoward result of this excessive rate of injection.

Most patients received but one or two liters of the Amigen solution. The most seriously ill were given more, the largest amount given to one patient was 26 liters during the course of ten days. In the two patients mentioned above, six liters a day were given for three consecutive days. We are unable to say how much more Amigen can be given per day as no attempt was made to increase the dose already mentioned, except that recently a patient received 25 Gm of neutralized Amigen per hour for eight hours, with no reaction and considerable clinical benefit. Experimentally, we have injected without reaction as much as 140 Gm of Amigen to a 10-Kg dog in 24 hours, with insignificant loss of amino-acids in the urine, this would correspond to 980 Gm in a 70-Kg adult, or about 40 Gm per hour, which is three to five times the rate we used in patients.

Findings—The clinical effects of the Amigen injections were carefully observed in each case and detailed records made thereof. Table I shows the general distribution of some of the data.

Pyrogenic Reactions Although chills and fever occurred in 15 instances, as can be seen by consulting Table I, ten of them occurred in patients receiving Solution No. 1, as already mentioned, this was the first solution employed and contained pyrogens in some of the distilled water used in its preparation. Of the remaining instances, three occurred in two medical patients, one with an acute respiratory infection, the other a severe osteo-arthritis, both patients had had chills previously. Of the remaining two instances both had chills but no fever and thus really should not be classed as pyrogenic reactions. On the other hand, at least one of the patients in this series had chills and fever following a transfusion before receiving Amigen. From this analysis, it seems fair to conclude that the few observed pyrogenic reactions (chills and fever) were not produced by Amigen, and that solutions which are not pyrogenic produce no reactions on the addition of Amigen thereto.

Other Reactions Two instances of urticaria were observed, one in a pa-

tient known to be alleigic to various substances. Since alleigy may be due to nonprotein materials, we may explain these two instances on such a basis, *i e*, to amino-acids or possibly mineral elements in the hydrolyzed casein. In both patients, the skin lesions responded to adrenalin and were followed by no sequelae. Flushing of the skin occurred in several patients, probably due to the specific dynamic effect of the amino-acids, which has been noted by other observers. As to temperature elevations, most of our patients were already suffering from fever before the amino-acids were injected, or were expected to develop fever as a result of the operative procedure. Study of these cases failed to show that Amigen was responsible for any significant temperature elevations. In many instances, the known specific dynamic action of the amino-acids, themselves, may have provoked some fever inasmuch as Shohl and Blackfan² found that the temperature elevations produced in infants by pure crystalline amino-acids and by hydrolyzed casein were alike. The chilly sensations observed in a few cases were, perhaps, also due to a specific dynamic action. Indeed, in two out of three cases in which the test was made, the basal metabolic rate increased during the course of the Amigen injections. Nausea and vomiting were rare in the present series, indeed, when expected as post-operative manifestations, Amigen seemed to minimize them. However, such symptoms are associated with the rate of injection, when Amigen is injected rapidly abdominal pain, nausea, and vomiting have been observed by Farr, Emerson, and Fletcher.³ In the patient mentioned above who received 100 Gm in less than an hour, these symptoms occurred, though there were no other untoward effects.

Phlebitis Careful observation revealed no instance in which 2.5 per cent Amigen caused any more phlebitis than similar solutions containing glucose alone. More recently we have prepared a neutralized Amigen solution (pH=6.5) which in stronger concentrations (5 and 10 per cent) seems less likely to produce phlebitis than similar solutions at a pH of 4.5.

Deaths Careful analysis of the deaths in this series of cases revealed no instance in which the Amigen could have been responsible. In each case the patient was in a critical condition before the administration of the amino-acids. They were given in these patients because they proved of such definite help in other similar cases which recovered. These were patients with serious gastro-intestinal disease, in poor nutritional and general condition, a situation which is not uncommon among the indigent.

Therapeutic Value Detailed objective evidence that amino-acids, when given intravenously, have a definite therapeutic value, was published in a previous paper from this clinic.¹ It was shown, for example, that excellent utilization of the injected material was achieved first because nitrogen retention was marked and persisted even during two weeks of therapy and second, because significant increases of the plasma protein concentration took place. Such detailed observations were not made in the present study. However, from the purely clinical point of view, there was ample evidence of the beneficial, even dramatic, effects of Amigen. In many cases it seemed clear that

the addition of the amino-acids to the parenteral glucose, after serious operations, tipped the balance in favor of recovery, although such impressions are, of course, difficult to prove. Significant was the fact that many patients volunteered expressions of subjective improvement in their general sense of well-being and strength, and this was confirmed by their clinical appearance and by the usual bedside observations.

It might be well, at this point, to make a few general remarks concerning the subject of protein deficiency. The practical application of this new method of parenteral protein therapy will be realized to a large extent by our ability to recognize protein deficiencies in surgical patients. The value of glucose is taken for granted because it supplies calories, yet body fat and tissue protein can likewise supply calories.

But there is no substitute for protein, indeed, one might say that if there is any secret of life it is bound up with protein which is the basis of all living protoplasm. In the past we have been lulled into a false sense of security about protein needs because of the presumed "stores" of protein in the body. Recent evidence has cast doubt on the practical application of this assumption. For example, it is now known that depletion of plasma albumin begins immediately after protein intake is stopped. Indeed, though hypoproteinemia is the only protein deficiency which can be recognized and measured clinically, its frequency is now generally admitted. Undoubtedly, other tissues suffer when their protein is depleted. The liver comes to mind, and something is known of this^{4, 5, 6, 7}. Manifestations of protein deficiency in other organs will doubtless be detected as time goes on. Indeed, one may even go further and say that certain acute conditions, such as burns, severe hemorrhage, shock, *etc.*, are in reality examples of acute protein deficiency since they lead to acute hypoproteinemia which the body cannot correct rapidly enough, and because fluid containing protein (plasma) is so therapeutically effective.

Plasma as a protein-containing fluid has become widely recognized within recent years as an important method of replacing lost protein, though it was used first in severe burns⁸ at the St. Louis City Hospital in 1935. As a means of supplying protein nourishment, though plasma leads to positive nitrogen balance in humans as shown by Kremen, *et al.*,⁹ it has two possible disadvantages. First are practical limitations, for example, the largest amount of protein which was given in 24 hours in the present study (300 Gm.) would require over 4,000 cc. of plasma or at least 16 donors a day. Second, are theoretical factors, *i.e.*, plasma replaces lost protein in the blood only, but must be hydrolyzed to amino-acids or small polypeptides by the body before it can be utilized by other tissues. In contrast, amino-acids injected intravenously are immediately available to all tissues. Indeed, if protein synthesis is rapid and much evidence seems to indicate that it is, an appropriate mixture of amino-acids should be built up into plasma proteins quickly enough to supplant in part, at least, the need for plasma and transfusions even in acute conditions, such as severe burns and hemorrhage. Work along this line is now in progress.

SUMMARY

Observations have been made of the injection of 1,013 liters of glucose solution containing a mixture of amino-acids (Amigen) in 312 patients. The injections were well tolerated and gave ample evidence of clinical benefit. Only two instances of urticaria were observed. The intravenous injection of a properly prepared solution of suitably hydrolyzed casein into the human in amounts averaging 8 to 12 Gm per hour for an average-sized adult is a safe procedure, and is the most simple and convenient way of supplying large amounts of protein nourishment parenterally. The far-reaching implications of this new method of therapy are briefly discussed.

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EPITHELIAL HEALING AND THE TRANSPLANTATION OF SKIN*

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STUDIES of epithelial healing and of the transplantation of skin have been made in close association with the clinical picture of the requirements and possibilities of repair in a large number of patients over a 17-year period. The reasons for wound healing or failure of healing, the spontaneous repair of donor sites of grafts, the behavior of homografts and many other points have been studied by microscopic sections of the tissues involved. Laboratory animals are not very similar to the human in skin and subcutaneous arrangement, and it is thought that human biopsies have been of the most direct value. The record has proven interesting and instructive and it is hoped that it may help furnish a histologic and physiologic basis for further investigation. To Dr Nathan Womack, thanks are given because of his help, interest, and patience in the protracted observations.

SPONTANEOUS HEALING OF LARGE OPEN WOUNDS

Wounds heal spontaneously by contraction of the surrounding edges, by filling in with fibrous tissue, and by scar epithelium going across from side-to-side. Skin is a complex organ and the epithelium is the only part of it that regenerates. The pad of derma that is really important in giving bearing protection does not regenerate, to any noticeable degree, and when a claim is made that a chemical will produce healing without scarring, the healing process is apparently not understood.

The thin scar epithelium that creeps across a wound by itself, and without any pad of derma to attach it to the subcutaneous tissue, may not be very serviceable as a bearing surface. It is thin, has no papillae, no hair follicles, no glands, and may form an excessive layer of keratin with nuclei remnants present far out in it. The latter finding may be evidence of a short life cycle of the cells associated with the continual wound stimuli of tension and repeated trauma. This scar epithelium may never become very firmly attached to the underlying fibrous tissue, so that large areas of it can be detached and lost by trivial injuries or infections (Fig 1).

Failure of healing may occur and is seen most often in circular burns of the extremities and wide open areas on the scalp. In such extremities there

Failure of healing may occur and is seen most often in circular burns of the extremities and wide open areas on the scalp. In such extremities there may be little or no upward growth of epithelium from the lower skin edge, so that the presence of even a narrow longitudinal strip of skin may be a big

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help in spontaneous healing. In the scalp, it has been conjectured that the follicles are so far differentiated into hair-forming structures that they do not revert to the production of surface epithelium so easily as elsewhere in the body. This is not true in the face, however, where rapid healing occurs, even

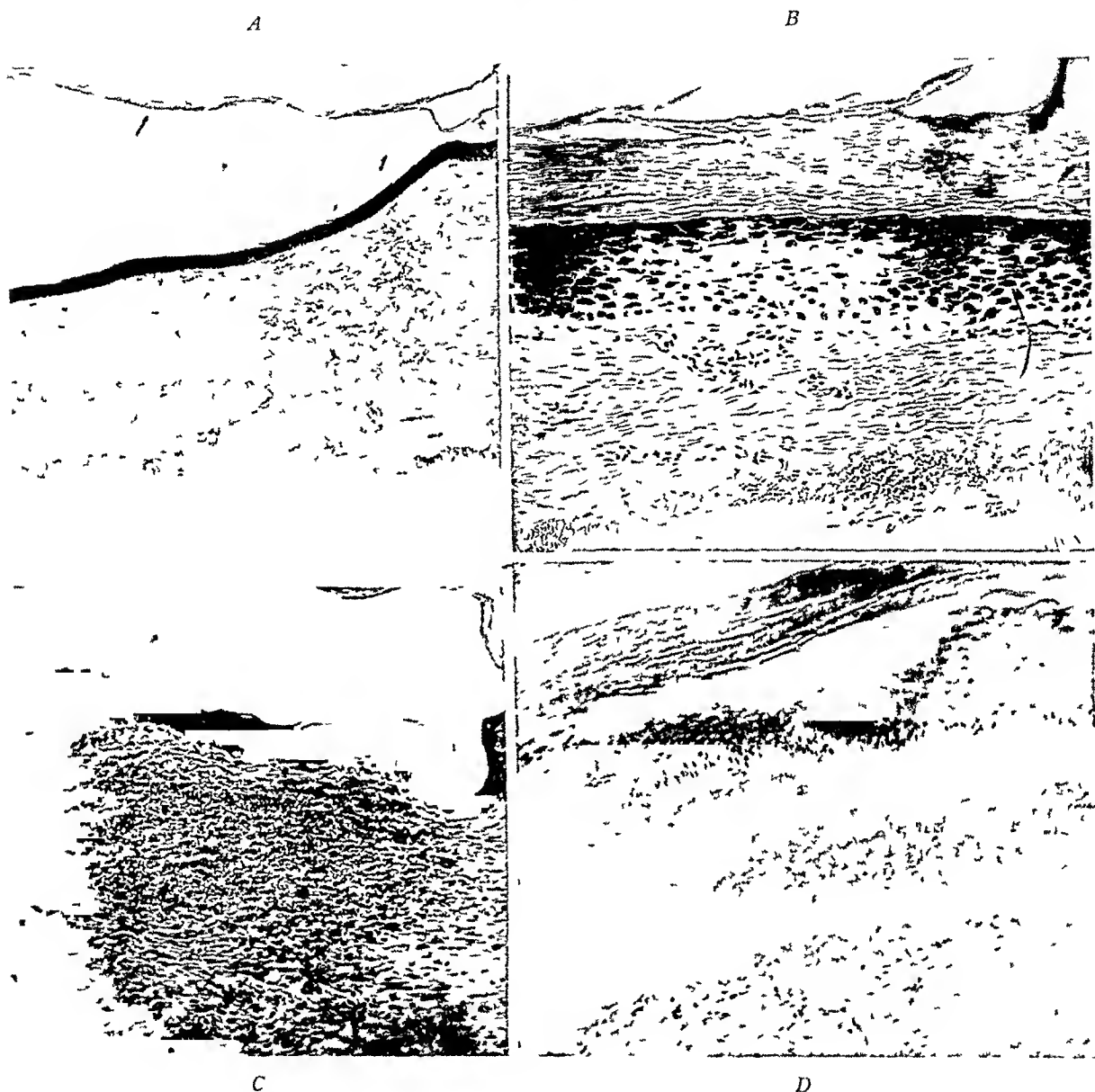


FIG 1—(A) Typical scar epithelial healing, with no dermal pad to attach it to the fibrous tissue under it (B) Same thing existing in a scar after 20 years. This does become "tougher" but retains the same microscopic appearance. (C) Fresh scar, with red blood cells collected interstitially, just ready to detach the surface scar epithelium. (D) Microscopic appearance of the frequent gross finding of detachment of scar epithelium by hemorrhage. Even slight trauma may cause a large surface loss from hemorrhage under this poorly attached epithelium.

in full-thickness losses, presumably from deep hair follicles that extend clear down into the subcutaneous tissues (in men) (Fig 2)

Individual variations in the growth of epithelium, aside from general nutritional factors, are marked. An occasional patient will heal a wide full-thickness loss and even get permanent bearing function. Others may heal rapidly but with so much dense, deep, fibrous scar that marked deformities are produced. These patients give about the most trouble of repair of any,

as this deep scar may have to be removed to allow normal function. Other patients seem not to grow any epithelium and may linger on over long periods, developing more pain and losing more body fluids all the time, and may die.

Studies of open wound (ulcer) edges have followed from the above considerations, and one of three pictures is usually found in them. (1) There may be no activity apparent at the edge at all, the epithelium simply thinning out and the stratum granulosum appearing to curve around to meet the basal layer, as though a permanent condition of open edge were to be established. This might be taken to illustrate an absence of response to the wound stimulus of the open area and usually occurs where there is little fibrous tissue laid down.



FIG. 2—(A) Failure of healing in complete, circular full thickness loss. (B) Edges quiescent, no growth from lower edge. (C) Complete healing following one thick split graft operation.

(2) There may be excessive keratosis with epithelial debris piled up along the edges, indicating a response to the wound stimulus by the short life of the cells, but failure of them to go on across the defect and effect a closure. (3) There may be a breaking up of the cells with apparent invasion of the deeper fibrous tissue, and it is presumably in this type of reaction that carcinoma develops. Carcinoma develops infrequently in comparison with the numbers of burns that occur. It occurs most often in areas that are prevented from collapsing, such as the scalp, or in large, dense fibrous ulcers that are repeatedly broken open.

Deep fibrous healing is presumably the only mechanism by which defects below the skin level may finally become closed, the area filling with granulation tissue that gradually changes to fibrous tissue. This dense tissue tends

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at times to defeat its own purpose by becoming so thick and avascular that it cannot support its own surface or any epithelium struggling across it. In some old leg ulcers, calcium may even be laid down in the scar and resemble sequestra roentgenographically. (Thus, of course, may come from adjacent periosteum.) It is the failure to remove this deep scar that accounts for many of the failures of grafts for leg ulcers and other wounds that have been open for a long time. Because of the thick, deforming dense fibrous tissue that may go along with rapid epithelial growth and produce early distortion, it is sometimes easier to repair the patient who makes little if any epithelial effort of his own, but who at least does not go into every possible kind of deformity

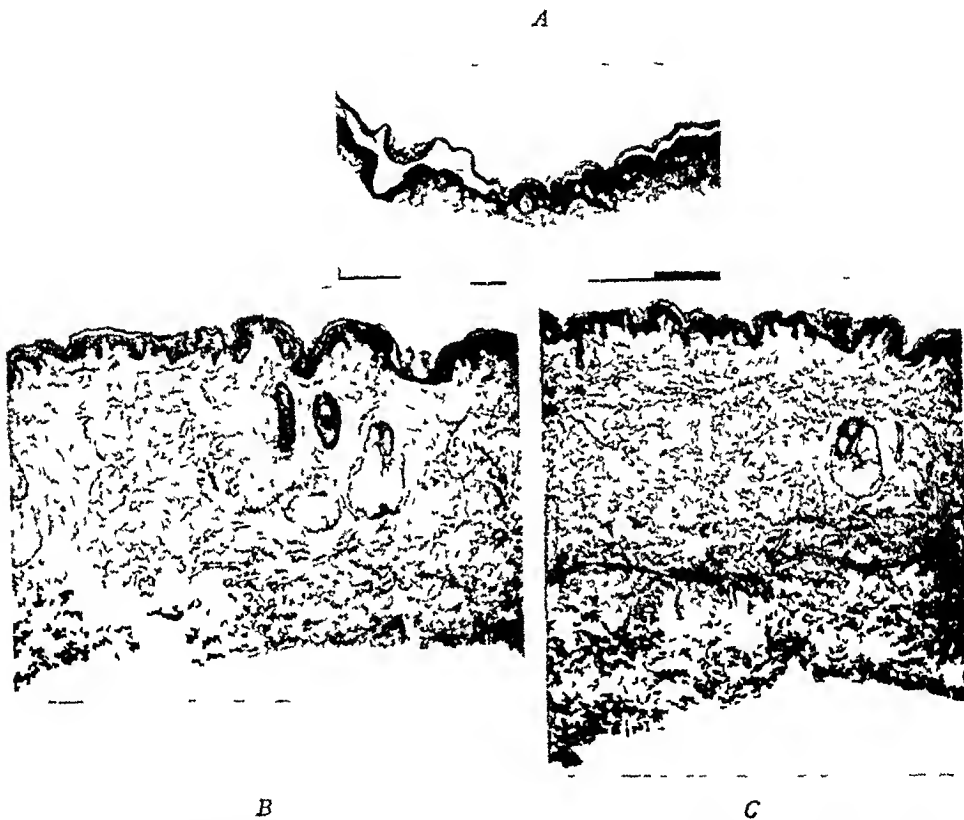


FIG 3—Three Types of Skin Grafts (A) Olher Thiersch graft, with practically no derma (B) Thick split graft of about 80 per cent of the full thickness (Used in 1932) (C) Full thickness graft

Generalized skin shortening is a term applied to areas that have healed, possibly with satisfactory surface, and which show no gross deformity but which do not permit normal function of complete flexion and extension. This is due to deep scarring and insufficient skin and is comparable to clothes that are too tight—the patient simply cannot bend around in his skin-envelope. The situation becomes especially bad if he puts on weight, as the dense blanket of scar will not distend for the new fat, and at times this thick, unyielding surface actually seems to form bursae over the deep fat. Notable examples of this have been published—one patient could not raise his arm without raising his leg, and another had not sat down normally for 26 years. The repair consists of opening suitable areas, either stretching back the edges or removing scar that is too dense, and filling the defect with free skin grafts^{2,9}

THE TRANSPLANTATION OF SKIN

Early Skin Grafting of Burns and Other Open Wounds—The main interest, generally, perhaps, is the problem of massive defects due to burns that have to be grafted to save life and prevent deformity, and in the later repair of contractures and deformities. Burns can usually be made clean enough for

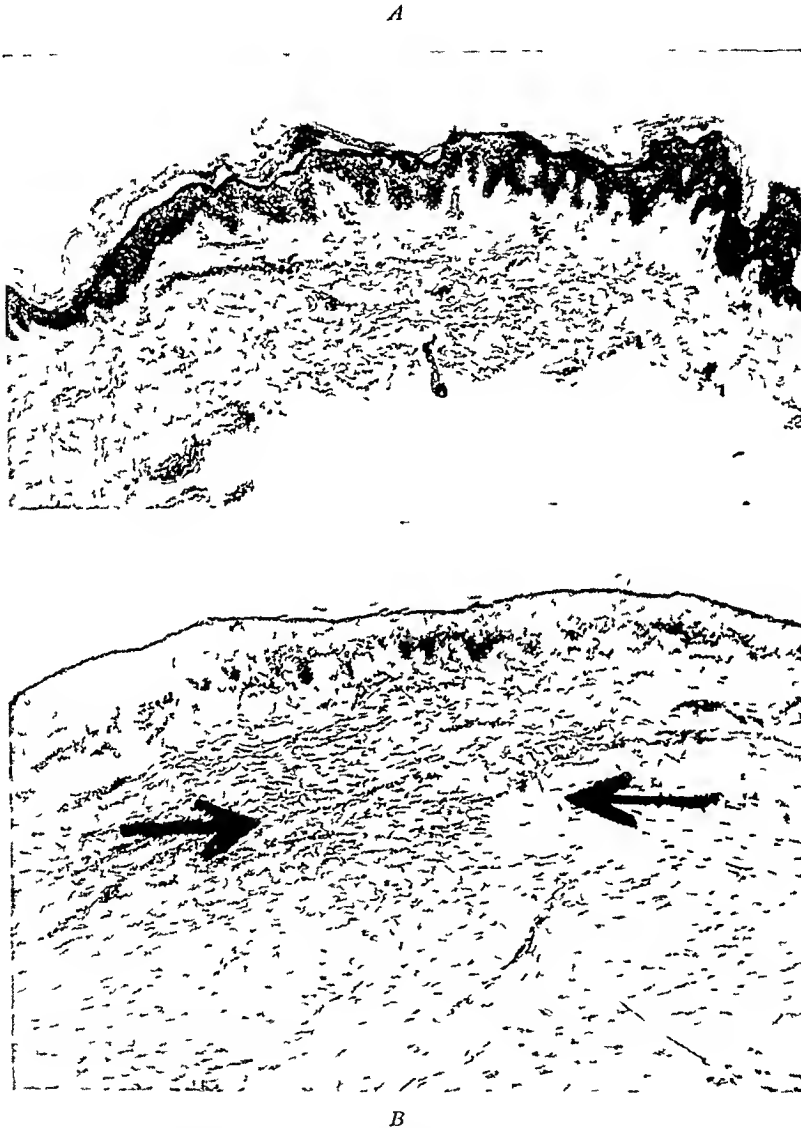


FIG. 4—(A) Thick split skin graft used successfully in repair of a burn. (B) Biopsy of same graft one year later. Arrows point to attachment of normal dermal pad to deep tissue. May be compared with Figure 1.

grafting in 20 to 30 days and as this plan has been followed for a long period, it can be extended now in war wounds, if suitable preparation can be carried out and tanned membranes gotten off early enough.

The immediate excision of burns and grafting, as suggested by Murat Willis many years ago, may have isolated applications, but cannot be a routine procedure for all burns. It would result sometimes in much good

tissue being sacrificed or in not getting rid of enough burned tissue and, because of this, a loss of the graft

Thick Split-Skin Grafts and the Relative Thicknesses of Other Types of Grafts—Figure 3 shows these grafts all taken from the same area in the same patient and magnified to the same degree. The split-graft is about 80 per cent of the full-thickness in this instance. When large areas have to be resurfaced, it is necessary to utilize only partial-thickness of the donor skin, leaving behind some derma containing portions of hair follicles so that healing can occur. When the full thickness of the skin is not taken, then it has been split in two and the most appropriate name for this type of graft seems to be "thick split-graft." The original Olber-Thiersch graft was too thin to be of much value, but almost any operator would, automatically, cut thicker grafts as he progressed in the work, so that the usual graft now used is one-half to three-fourths of the full thickness of the skin. Various other names have been employed to describe this graft.

The actual thickness of whole skin varies greatly in age, sex, race, various degrees of nutrition, and in different areas of the body. The skin is also of different character in various areas. On the back, for instance, the epithelium is relatively thin but the derma is so thick that full-thickness grafts from this area can hardly be counted on to survive. Burns in this location are seldom completely through the derma and tend to heal readily. Split-grafts from this area do not need to be as thick, relatively, as from other areas, and because of this, as many as five "crops" of skin have been taken from the same donor site at intervals as short as 19 days. The palm is just the opposite, with a specialized type of epithelium that produces a thick keratin layer for protection and has a thin derma without hair follicles. It heals very poorly following burns and even rather superficial ones may produce marked deformity, especially in children. The same is true of the sole.

Importance of the Dermal Pad of a Skin Graft—To show the importance of a pad of normal derma between the underlying base and the surface epithelium, the split-graft in Figure 4 A was followed clinically for one year, at which time the result was satisfactory, and a biopsy was taken. Figure 4 B shows the graft after one year, appearing as normal skin with normal papillae, no excessive keratin—indicating a normal life cycle of the cells and absence of wound stimulus. The epithelium is attached to what is left of the fibrous base by the pad of derma included in the graft and a normal bearing-surface is produced that can withstand the usual trauma of getting around. This may be compared with Figure 1 A and B, in which the scar epithelium on a scar base is seen, and the comparison is the essential difference between spontaneous scar epithelial healing and healing by grafts.

Cutting Thick Split-Skin Grafts—These grafts may be cut in several ways, the main essentials being a long sharp knife and some method of producing a diaphragm on which to cut. The diaphragm may be produced by pressing down, as with two large spatulae, or lifted up as with tenacula, a vacuum suction retractor, or with glue, as on the dermatome. Each method has its

advantage, according to the availability of the skin in relation to size and nutrition of the patient. For large defects, the grafts should be cut as large as necessary for ease of repair—on a large person, ones 18x5 inches are possible, and grafts 36x4 inches have been cut free-handed with a long knife (Fig 5 A, B). The dermatome may be useful in obtaining smaller grafts from more difficult areas, such as over the thorax, or from small children, where its size (8x4 inches) may be sufficient. One has to be careful not to

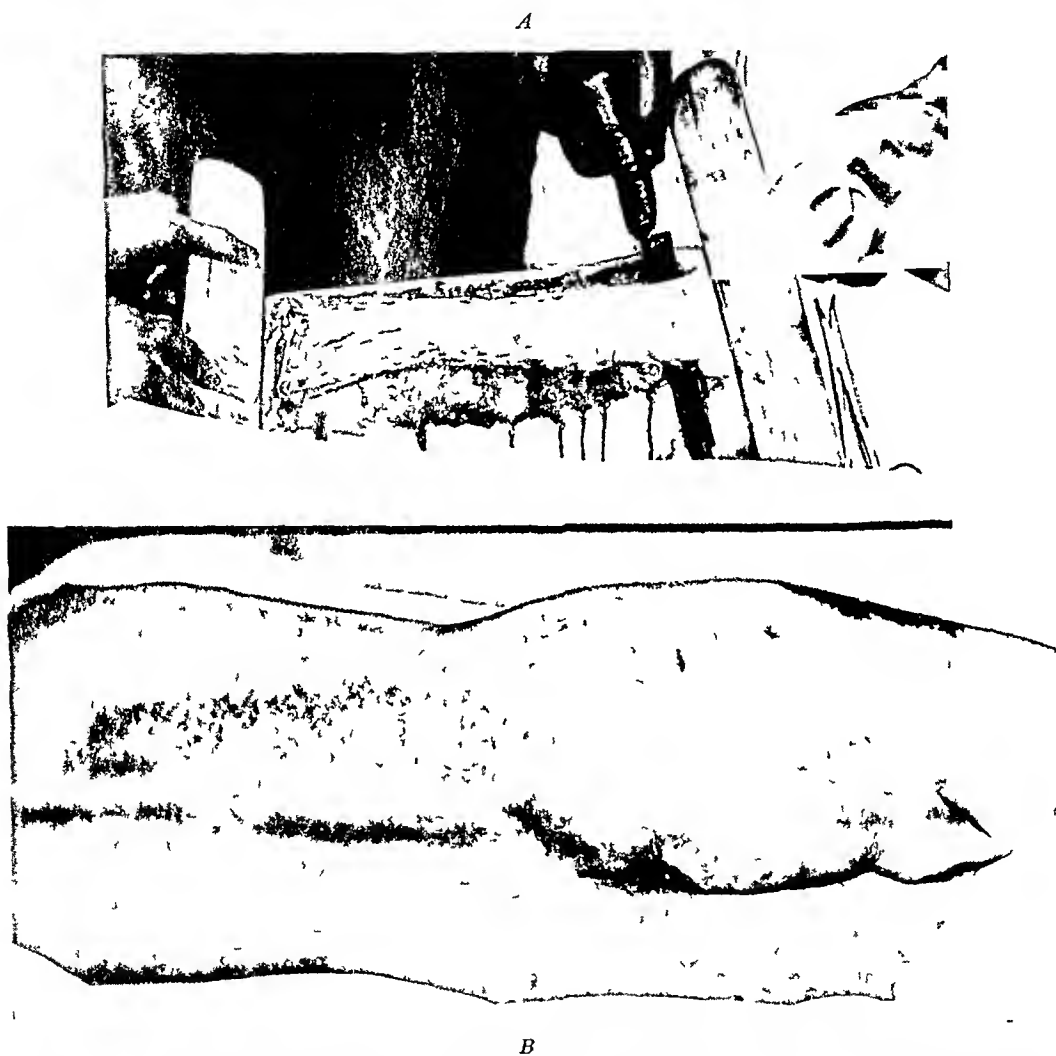


FIG 5—(A) Free hand method of cutting thick split graft, about 75 per cent of the full thickness (11 x 4 inches). (B) Larger grafts are available in large patients. Healed sites shown of one graft 36 x 4 inches, and one 30 x 4 inches.

set it so deep that the full thickness of the skin is taken, or so thin that the graft cannot be detached from the drum. The free-hand method, when possible, is usually the fastest and safest method, and with some practice the thickness of the graft can be graduated and certain designs roughly obtained (Fig 5 A).

Preparation of Base for Split-Grafts and Where They Will Grow—Grafts may be put directly on the surface of open wounds if the granulations are bright red, flat, firm, and not edematous. However, if feasible, the granula-

tions are *sliced* cleanly off with a graft knife. They are not scraped, as this seems definitely to interfere with the take. In healed areas, especially if they have recurrently broken down, the scar epithelium and deeper fibrous tissue are removed down to a thin scar base so the area can relax. It may be necessary to open entirely through the scar to gain correct position of the parts, but this should always be done very carefully if there is any possibility of exposing tendons by sudden force. In Figure 4 B, the deep scar that has been left is seen under the graft.

Grafts will not grow on tendon or bare cortical bone (without periosteum), but may carry a lateral blood supply of their own across small areas of these tissues when exposed. This is important in work about hands because, if one goes very carefully, one can stop any tendon exposure before it is over 1 cm., and this is about the limit that the graft can be expected to carry over.

When put on fat or muscle, or uneven scar bases, the grafts will grow, but will later show every irregularity and there will be new scar tissue laid down that may contract the surface markedly. This has been said to be due to contraction of the graft, but it is probably from contraction of the bed under it.

Sulfanilamide may be dusted sparingly over the bed for the graft without measurably stopping the growth, but any excess certainly would be contraindicated and it cannot be expected to replace any precaution of cleanliness nor to prevent loss of a graft if a severe contamination has occurred.

The preliminary preparation is as important as any step in the repair of a large open wound and consists mainly of open drainage, soap and water, local sulfonamides, and daily débridement. Rest, elevation, and pressure dressings are fundamentals that cannot be omitted, but are only mentioned here for the sake of completeness. Ointments on areas to be grafted are used on fine-mesh gauze during the preparation but none should be on the wound at the time of operation, and if suspected, ether should be used as a solvent. Grease left under a graft almost precludes its growth. Somewhat of a reason for this has been noted (by others) in tissue cultures, in the finding that on the addition of a drop or two of mineral oil to a tissue culture, taxis of the cells ceases.

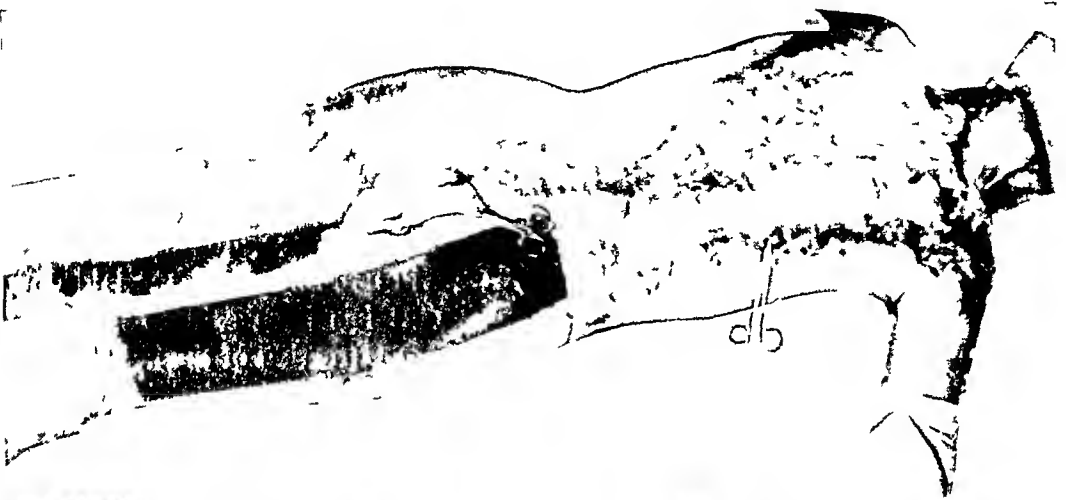
Pressure dressings on skin grafts are almost an absolute necessity (an occasional graft laid on and not protected might survive, but one could not run a service that way). The medium of pressure distribution that seems most suitable is white cotton mechanic's waste. It has to be held on the same as any medium does and it is, therefore, the final bandage that produces the pressure (Fig. 6). Firm pressure is an excellent antiseptic, apparently by preventing the accumulation of surface fluid and keeping down edema, and its use has been noted in the hieroglyphics of the Edwin Smith Surgical Papyrus. Pressure dressings are also used on fresh burns when possible.

EPITHELIAL HEALING

The Epithelial Healing of Donor Sites of Thick Split-Grafts—This provides an especially good opportunity for gaining information of epithelial

healing in general. Large areas are denuded under sterile conditions and the influence of any agent on the rapidity of epithelial healing can be readily noted. The resemblance to a superficial burn or to a deep abrasion is evident. The ability of these to heal promptly makes possible the transfer of 100 to 250 square inches of skin at one time and it is most important to make sure that

A



B

FIG 6—Fine mesh gauze next to donor sites and over grafts. Massive pressure dressing using cotton mechanics cast to protect both donor sites and grafts. Massive thick split grafts 210 inches in one operation. One graft, 16 × 4 inches, from shoulder to buttock. Others over back, arm and neck.

this healing does occur by using extreme care in dressings and protection (Fig 6)

Dedifferentiation of the Hair Follicles in the Healing of Donor Sites—In the healing of donor sites, the deep glandular epithelium in the derma spreads out over the surface and entirely recovers it in six days, and in six more days, dressings can be left off. In fact, only one dressing is done on the tenth to the twelfth day. This process is a sort of "dedifferentiation" of the cells of the hair follicles, as far as we have been able to determine, and a gross observation

in substantiation of this is the fact that on the palms and soles, where there are no hairs, healing is slow

Microscopic Appearance of Epithelial Dedifferentiation—The whole process can be studied microscopically in biopsies taken at intervals (Fig 7) Healing is complete by the sixth day, and by the ninth day, conversion to squamous epithelium is so complete that papillae are formed and some keratin



FIG 7—Healing of Donor Sites of Thick Split Grafts (A) Biopsy, two day old donor site—no surface epithelium (B) Two day old biopsy showing deep follicle but no surface coverage (C) Four days later, or sixth postoperative day showing complete coverage with squamous epithelium (D) Ninth day, with normal appearing epithelial surface

is being thrown off. This process is apparently the reverse of the original formation of hair follicles. It is also something like a reversal of carcinoma formation, and it was thought that a somewhat similar picture might be found if enough healing donor site biopsies were done. This has not been entirely clearly shown because the cells go out so rapidly and orderly, but suggestions of it have been found.

Careful Protection of Donor Sites to Obtain Healing—It is apparent that this process is a very delicate one and that irritation of any nature, chemical, bacterial, or mechanical, will prevent healing. When this does occur, the healing period is changed from ten days to eight or ten weeks, and whole

areas of the derma seem to melt away. It is evident that extreme care should be taken not to damage these cells and, therefore, no strong chemicals are put on the area. It is dressed immediately to protect it from trauma and contamination with fine-mesh grease gauze (No. 44 gauze), held firmly in place with overlying pads, adhesive and bandage that cannot slip. If any openings have been cut through the derma, they are carefully closed before the dressing is applied (Fig. 6).

When large areas are denuded, the additional bleeding and fluid loss may be considerable and whole-blood transfusions are often advisable.

The application of fine-mesh gauze to these and all raw surfaces is a fundamental of extreme importance to allow healing to progress smoothly and, on granulating surfaces, to avoid growth of them through the meshes of coarse gauze.

Rapidity of Healing and Multiple "Crops" from Same Area—Split-graft donor sites usually have to be guarded a week or so longer after the 10 to 12 days, but a second "crop" of grafts has been taken as soon as 10 days after the previous "crop," and five "crops" have been taken from the same area. There is a marked variation in patients in their rate of healing. One patient, for example, who healed his donor sites rapidly and had four "crops" from the same area, did not make any new lateral spread of epithelium over his burns. Negroes are ideal patients for grafting, grafts seem to grow on them almost regardless of technic, but they are a little slower in healing their donor sites. This may be because they tend to have less hair.

The Skin of the Back—This early and repeated healing where multiple "crops" are taken has usually been from the back, where the derma is thick, but care is taken not to cut too deeply, the skin does finally wear out and the last "crops" are not as nice to use as the first one.

The possibility of enough skin for repair in each burned patient is usually present if the above precautions are taken. The graduation of the thickness that is possible in free-hand cutting is probably the safest way of avoiding trouble, and of insuring the possibility of multiple "crops" from the same area.

Saving a good donor site on badly burned patients is important for obtaining smooth full-thickness grafts when final operations are to be performed about the face and neck. A thigh or the lower abdomen may be left for this work, but it is frequently found that someone has removed pinch-grafts right out of the center of these areas.

HOMOGRAFTS

Homografts are usually thought of at this point, when the possibilities of the patient having enough of his own skin are considered. These grafts will take almost universally even without regard to blood grouping. In grouping one series of 26 down into the M and N groups (with Dr. Francis E. Holford) no relation was found either to the take or to the length of persistence. However, they will not persist in place over 10 to 11 weeks, and usually begin to disappear at the third week by a sort of solution of the graft, usually without pus formation.

Biopsies taken early in this process of solution show interstitial edema, with slight cellular infiltration, as might be seen in an urticarial wheal. Later, the interstitial edema is less striking, and the cellular infiltration becomes heavy, consisting chiefly of round cells with many eosinophils and some polymorphonuclear cells. This heavy cellular infiltration coincides with the disappearance of the various dermal elements and epithelium in scattered areas. Grossly, the graft has numerous tiny areas of loss and appears "moth-eaten"



FIG 8—Emergency Dressing of Wounds in Homografts (A) Extensive burns of arms, legs and face (B) Whole arm healed with homografts from father. At same time, permanent autographs put on hand and face

at this time. These areas increase in number and coalesce until final complete solution of the graft occurs. It would appear that the proteins in the homograft are antigenic and that the host requires about three weeks to build up a maximal allergic response to them. If a second crop of homografts from the same donor were applied to the patient at this time, one would expect almost complete failure to take. By the same reasoning, any previous attempts to "desensitize" the patient to the donor's skin proteins would probably decrease the chances of take. Conversely, attempts to "denature" the antigenicity of

the proteins in a homograft, or to change them by previous immersion in the patient's serum, have not proven clinically successful in skin grafts

The emergency "dressing" of wounds in homografts is employed occasionally as a life-saving measure and in intractable children. Large sheets are taken from the donor and applied quickly, about as a dressing of the wound. The effect is stopping of pain, and the necessity of care, improvement generally, cleaning up locally, so much that there may be a marked stimulus in the patient's own epithelization, have been misinterpreted by some observers as a permanent survival of the homograft (Fig 8)

According to Dr Leo Loeb, no two individuals are exactly alike, and with our present knowledge, there is no use to expect a homograft to survive. Much work has been done along these lines, and if the problem could be solved, one of the greatest possible advances would have been accomplished. Skin is an organ and not just the epithelial element, so that it probably cannot be grown in a foreign body any more than any other organ and persist.

Homografts in identical twins, however, have been shown to survive, and if a twin were burned, the other one could probably be used satisfactorily.⁴

Delayed or refrigerated grafts are possible and have been used clinically occasionally, and experimentally in animals, and from humans to animals, but there is not much clinical use in the procedure at present, since the patient is always on hand to supply his own skin, and the obtaining of the graft is the minimal part of the procedure. In one case a successful full-thickness graft on the neck had been stored in an ice-box for forty-eight hours, as far as is known, this is the first clinical instance of the use of this procedure. One can conjecture all sorts of storage plans and tissue culture plans for grafts, to be used in war time, but final success has not been attained.

(Illustration of this part and eight other figures omitted.)

LATE COURSE OF THICK SPLIT-GRAFTS

Sebaceous collections may occur to an annoying degree, possibly because the cut glands secrete backwards. At least it appears this way since multiple large collections may develop. Their importance is that final healing may be delayed, and if the large collections become infected, excoriation or even loss of part of the graft may occur. There is usually a deep layer of epithelium under these collections, so that if they are opened and expressed, and any overhanging edges trimmed away before infection causes damage, serious loss is avoided. This occurrence is one of the marked variations, some patients not showing it at all and others showing it badly, regardless of how thick the graft is cut, however, full-thickness grafts never show it. This also may be due to small areas of the original skin being left behind and the grafts having been put over them.

Persistence of function of skin grafts over long periods of growth has been studied and it seems that grafts do grow or stretch out, so that if a graft has been successful at the beginning, it is apt to remain so. If any lack of skin for ease of function (skin-envelope) is noted, suitable openings can be made and more skin let in.⁹

Satisfactory function of grafts is meant to include "(1) Enough skin for free movement, (2) moderate looseness, (3) ability to withstand the usual trauma of getting around, and (4) the development of normal sensation. Full normal sensation usually develops in free skin grafts and is influenced by the amount of deep scar that is left and, of course, is dependent on the presence of sensory nerves in the area."

Metaplasia of grafts (and flaps also) does not take place and, therefore, a really normal sole of palm, for instance, cannot be restored. The skin of

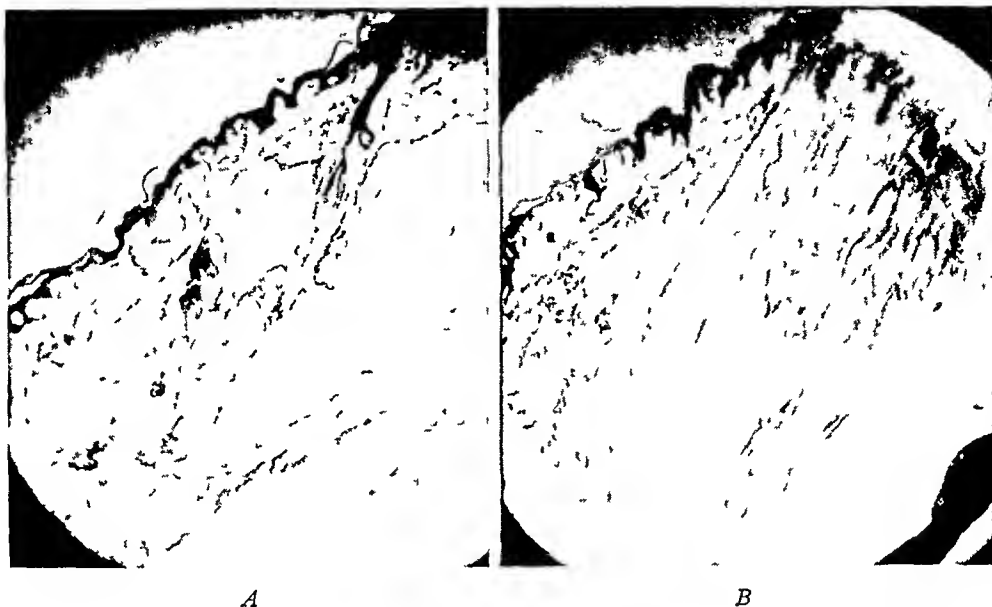


FIG 9—Failure of Metaplasia of Skin Grafts. (A) Biopsy after one year—from graft in orbit. Graft is still skin grossly and microscopically. (B) Biopsy after five years—from inside larynx. Graft is still skin, with hair growing from it.

each of these areas is specialized to the point of being an organ, the microscopic structure is different from birth and the peculiar bearing qualities are not developmental. "A graft or a flap on a sole may make calluses (or even annoying warts) but it will not metaplasia into true skin or subcutaneous tissue of the area. They always have to be protected and the wart formation guarded against. If hair is transplanted, it will continue to grow, except that it may be worn off.

"Skin grafts transplanted to normal mucous membrane surfaces, such as the mouth, larynx, and eye socket, show no evidence of a change to a mucous membrane. The skin simply persists as such and even raises hair in these areas, if there are any functioning follicles in the graft" (Fig 9)."

Lines of Investigation—At this time, when burns and grafts demand a good deal of attention, it is desirable to have the whole subject, including objects, reasons, possibilities and limitations, put on a plane approaching other surgical subjects. Important lines of investigation are (1) Information to be gained and correlated from tissue cultures, (2) chemotherapy in relation to preparation of wounds and at time of operation, (3) refrigeration of grafts before being applied and of the areas after operation, (4) development of occlusive dressings that are transparent and removable, (5) prevention of

burns, (6) earliest possible replacement of skin following burns, (7) improvement in dressings and pressure media, and of air pressure on wounds plus burns, (8) simplification and ease of obtaining split grafts, (9) possibility of getting homografts to survive, and (10) utilization of delayed grafts

Much has been accomplished, but it is apparent that there is room for vast improvement

PREVIOUS PUBLICATIONS

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- ¹⁰ Thick-split Skin Grafts in the Repair of Burns Surg, Gynec, and Obstet, 73, 265-267, 1941
- ¹¹ Skin Grafting of Burn Deformities (Army Manual, to be published)
- ¹² Massive Repair of Burns with Thick-split Grafts ANNALS OF SURGERY, 115, No 4, 658-674, April, 1942

DISCUSSION—DR SUMNER L KOCH (Chicago) There were so many things Doctor Brown could not include in this rather brief discussion, that I want only to emphasize just a few of the principles that he has suggested and repeat them, because we think they need to be repeated from time to time

First of all if there has been a whole-thickness loss of skin no dressing will bring about healing The only way that raw surface can heal is by ingrowth, the slow ingrowth of epithelium or by replacement

Second the more quickly replacement is brought about, the less will be the contracture that develops All of us I am sure see, too often patients left for long periods of time in the hope that spontaneous healing will occur While it does go on very slowly, difficult and serious contracture is developing and increasing and, of course, the longer it goes the more difficult it is to overcome

Third Doctor Brown has not had time to talk about the importance of securing a clean field He has suggested it, and he has referred to it in his paper, but to secure a successful result one must have a clean field Many advances have been made recently, particularly in methods of securing grafts, and all of us have seen very beautiful grafts taken by various methods Too often the unthinking surgeon forgets that the field has to be clean or the graft cannot live Nothing that I know of helps so much to secure cleanliness of that field as simple surgical cleanliness and avoiding adding infection to the raw surface that is to be covered

Again surgeons so often forget the importance of not adding infection to the open wound as they are trying to transform it into a clean wound They forget that the more serious potential sources of infection are the surgeon's hands and his instruments and, most of all, the uncovered mouth and the unmasked nose I never have had the opportunity of going to another hospital to see a patient with an extensive injury and been offered a mask to cover my face before examining the large wound that was distressing the surgeon I

think it is something that we have to repeat over and over again to our students and our house officers, that just as in the operating room, where everyone admits the importance of preventing infection, so in the ward and in the patient's room those same precautions must be taken, and that if we are going to secure clean wounds we must prevent adding infection to them throughout the course of treatment

DR NATHAN WOMACK (St Louis) There is one thing about Doctor Brown's paper that I would just like to stress, and that is his demonstration of the extraordinary rapidity with which apparently perfectly normal epidermis can be formed in five or six days from squamous epithelium. If it is sectioned longitudinally and separated with a clothespin, one sees a very marked resemblance to skin but functionally it does not resemble skin. It does not resemble it in pigmentation. It does not resemble it in its metabolism.

It will be very interesting to observe what happens to some of these donor sites that Doctor Brown has under observation many years from now, whether or not the function of the stratified squamous epithelium of the skin is picked up as well as its morphologic structure.

One other thing. I think the preservation of potency we see explains the marked variation that one sees in the other direction, that is, the formation of tumors.

The fact that cells are able to perform other functions than those they are normally supposed to do, such as squamous epithelium in the bronchus, and squamous epithelium in the gallbladder, explains some of the multitudinous morphologic experiences and some of the skin cancers that Doctor Brown has been talking about.

DR VILRAY P BLAIR (St Louis, Mo) May I emphasize a point that Doctor Brown brought out? I did not catch that he said it directly, though he demonstrated it. That is the futility of homografts in preserving the vitality of the patient and bringing about an early condition where one can put on the autograft. Especially in young children, that is very useful. A child is badly burned. You take the graft from the mother and put it on, knowing it is not going to last, but by the time it has disappeared it has fooled many people into reporting in the literature that they have had permanent results, which I do not believe they ever did get.

SKIN REMOVAL IN RADICAL MASTECTOMY*

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THE SURGICAL TREATMENT of cancer of the breast was in a quite unsatisfactory condition until 1894, when Halsted and Willy Meyer published their papers on radical mastectomy. Halsted advocated "wide" excision of skin with removal of the breast, the pectoralis major and minor, thorough dissection of the axillary lymph nodes, and immediate skin graft. This had a profound influence on the surgical treatment of breast cancer. His original operation has been followed by many to this day, even though Halsted later somewhat changed his own technic.

In the decades that have since passed, there has been quite a general acceptance of the complete removal of the breast, the thoracic portion of the pectoralis major, the pectoralis minor and the axillary contents. There has not been, however, an agreement on the best method of treating the skin over the breast.

Halsted advised the "wide" removal of skin of the breast including the nipple and areola. His method seemed to indicate an incision through the skin down to the deeper subcutaneous tissue, followed by peripheral dissection to expose all of the breast along with the muscles and axilla. He then carefully closed off the dead space in the axilla with interrupted silk sutures, to leave a raw area that was covered by immediate skin graft. Halsted had operated upon 50 such cases when he made his report in 1894. Of these 50 cases, 31.9 per cent developed local recurrences.¹ From a review of the literature, the writer has been unable to find any statements of the measurements of the skin removed.

Handley,² in his study of cancer of the breast, had come to the conclusion that the growth spread chiefly by permeation and lymphatic emboli. He contended that the cancer spread in a ringworm-like process in the deep subcutaneous level just superficial to the fascia over the muscles, and that it was only in a late stage that extensions from this level went up vertically to the skin, like a bubble coming to the surface of a pond. He felt that there was no spread by permeation beneath the cutis. Therefore, he believed that it was not necessary to sacrifice a "wide area" of skin such as Halsted had advised, but that a smaller area could be excised with wide peripheral dissection in the subcutaneous level, superficial to the deep level in which the cancer spread by permeation. In accordance with this observation, he was content to remove a diameter of four to five inches of skin by a circular incision, with the tumor as the center. He was usually able to approximate the skin edges by a plastic type of repair at the completion of the operation. In this way he avoided the skin graft to the bare chest wall.

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

It is accepted that cancer of the breast begins as a local lesion, and that it first spreads by *infiltration*. Undoubtedly, in some of our cases this was the only stage that the growth had reached. But because of our known inadequate methods of gross and microscopic examination, it has been felt necessary to perform a radical mastectomy. The next steps in the spread of the growth have been by *permeation* and *lymphatic embolism*. Both these methods probably occur at the same time, but vary in incidence and degree, if one is to judge by clinical and pathologic experience. For it is known how variable is the relationship between primary growth and axillary metastases. Fortunately, *blood embolism* does not occur often, otherwise there would be little indication for more than local surgery.

All these methods for the spread of breast cancer are accepted in principle, and there has been but little disagreement except on the subject of permeation. As I see it the "Halsted school" believes that the cancer spreads by permeation in the cutis, and that, therefore, a "wide" portion of skin must be removed. Secondly, we have a school of thought, led in New York by Hugh Auchincloss, that agrees with this Halsted school but believes that it has not gone far enough, as the spread peripheral to the excised skin is in the tissue immediately beneath the cutis. Therefore, such a careful dissection of the skin must be made as to leave no fat attached to the under surface of the skin. And thirdly, we have the Handley belief that the cancer spreads in the deep subcutaneous tissue, so that when the skin or immediate subcutaneous tissue is involved, it is due to involvement of vertical lymphatics to the skin from the deep tissue.

The pathologic evidence for each belief has been difficult to establish so that different opinions have been able to persist. On clinical grounds, however, one may draw some conclusions. The proponents of these theories have enthusiastically gone into battle to prove their contentions. The Johns Hopkins Hospital report claims that, in every way, wide excision with skin graft gives superior results to the plastic closure technic. Auchincloss³ states that with his more radical technic, "local recurrence is rare." Handley,⁴ in 1930, said "Broadly speaking, local recurrence was nearly abolished."

Freedom from recurrence, or persistence of the disease in the local area, is said to be a good measure of the thoroughness of the radical procedure. Evidence of the disease beyond the field is no reflection on the surgeon's technic.

In the case of local recurrence, one must presuppose that malignant cells have been left in the skin and in the raw area, with a chance to grow and later appear. On the other hand, one must also admit that by lymphatic embolism, cells may be deposited in the intercostal lymphatics to spread locally. In the same fashion, the lymphatic emboli may go, and I believe frequently do go, to the lymphatics associated with the perforating branches of the internal mammary artery. So it seems to me that some of these nodular recurrences in the intercostal space near the sternum, and occasion-

ally some of the others deep beneath the skin, have no part in the proof for the indications for skin removal

Local recurrences in the scar and the skin of the immediate chest area are of great significance. But when they appear in skin edges after a 25 cm diameter of breast skin has been removed, how shall we judge it? Was the case inoperable primarily—or, when the recurrent nodules appear in the local skin after ten or 15 years, along with lung or bone metastases, is this due to a faulty lack of sufficient skin removal?

It is the fashion in some circles to decry "statistics," as unworthy of notice because of the variabilities in the nature and course of cancer of the breast. It is admitted that one cannot argue from the general to the specific in each case. It is also true that dogmatic traditional statements of procedure should not be accepted on mere impressions. The collection and study of the operation, the pathology and the postoperative course of patients over at least five years, gives an indication of trends and indications for procedure that are worth while.

For this study the writer has taken the records of the cancers of the breast that have been subjected to radical mastectomy at the Roosevelt Hospital in the period January 1, 1922 to December 31, 1936. For the purpose of this review, all cases that had recurrence in less than 5 years, and later, were included. All cases that were well and free from the disease but lost in less than five years were excluded. In some of the articles in the literature, on local recurrence, the authors have included too recent cases. No time was allowed to develop recurrence.

This is a report of 254 cases, 238 with plastic skin closure, and 17 with skin graft.

Of the 238 plastic skin closures, 137 had proven axillary metastases, 43 had local recurrences, including three parasternal nodule recurrences (31.5 per cent).

Of the 238 plastic skin closures, 101 had no axillary involvement (in pathologic examination). Eleven had local recurrences, including four parasternal nodule recurrences (10.8 per cent).

Total—238—54 local recurrences (22.6 per cent), excluding seven parasternal recurrences (19.7 per cent).

Of the 17 skin graft cases, 14 had axillary metastases, with five local recurrences (35.7 per cent), while three had no axillary metastases, with one local recurrence (33 per cent).

TABLE I

PERCENTAGE OF RECURRENCES IN 238 CASES WITH PLASTIC SKIN CLOSURES

No of Cases	Local Recurrence	Per Cent
137 with axillary metastases	43	31.5
101 without axillary metastases	11	10.8
<hr/> Totals 238	<hr/> 54	<hr/> 22.6
225 graft cases (Johns Hopkins Hosp.)	79	35

SUMMARY

The writer, together with his associates, had been intrigued by the work of Handley. It was felt that the plastic closure was preferable to the skin graft if it did no harm to the patient. In the period included in this paper, the policy of following out Handley's technic has been followed. It will be noted that in 17 cases immediate skin graft has been necessary. This is due to the fact that we insist on removal of at least 15 cm. of skin at the narrowest diameter, and often more if the growth was large. By liberal undercutting, it is usually possible to approximate the skin without undue tension, but in the patient with small breasts this may not be feasible. On the contrary, it is easy to close skin edges primarily in large breasts, even though a diameter of 25 or 30 cm. has been removed.

We wish to emphasize the fact that in the cases with local recurrence death was not caused by the local recurrence but by the cancer metastases outside the operative field. Furthermore, in the late skin recurrences, we have been impressed by the simultaneous appearance of evidence of cancer outside the operative field. For this we have come to the conclusion that we have not lost any patient because we have failed to make a wider excision of skin.

We feel that the "skin graft school" has taken an empirical attitude that is not supported, as yet, by results.

CONCLUSIONS

From our investigation we have come to the conclusion that (1) local recurrence is fairly frequent, (2) a follow-up over many years will show increasing percentage of local recurrence, and (3) our method of skin removal is reasonably radical. In the local recurrences (especially in the skin) that occur with this method, the failure is not due to the method but to the pathologic fact that the cancer is already widespread, without our knowledge, and beyond the reach of surgery.

A comparison of our results with those of other "schools" is difficult because of the paucity of information on this subject in the general literature. A notable exception to this has been the exhaustive study of the Johns Hopkins Hospital cases by Lewis and Rienhoff. Reference to this report is made in Table I.

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TISSUE REACTION TO RIBBON CATGUT AND PRESERVED OX FASCIA LATA STRIPS*

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IN A good many publications Koontz^{1, 2, 3, 4, 5} has pointed out the advantages of preserved ox fascia strips as suture material in various conditions. In 1932, he⁶ showed the differences in tissue reaction to catgut and kangaroo tendon as compared with ox fascia strips. The former are either soon absorbed or become friable and lose their tensile strength. Both catgut and kangaroo tendon cause a marked reaction in the tissues—with a wet wound, an abundant cellular reaction, and marked leukocytic infiltration. This is more marked in the case of kangaroo tendon than in that of catgut. On the other hand, preserved ox fascia lata strips show no tendency to be absorbed in the early months (eight months) that they have been studied, and there is no cellular reaction around them. There is, however, a reaction on the part of the surrounding fibrous tissue—new fibroblasts growing in among the implanted connective tissue fibrils of the ox fascia lata strips, becoming incorporated with them, and revivifying them by furnishing living cells and blood vessels which wander in between the old inert collagen fibrils.

In 1933, Lowsley and Bishop⁷ introduced the use of ribbon catgut for repairing nephrotomy wounds. The following year, Lowsley⁸ reported an operation for ptosis of the kidney, using the same material, and stated that the kidney stayed where it was placed. He has also used the material to plicate the bulbocavernosus and ischiocavernosus muscles for the surgical relief of impotence in man.^{9, 10} Lowsley has also used ribbon gut for the relief of urinary incontinence by placing an encircling band of it around the urethra.¹¹ Experiments in animals, in connection with this operation, showed that the ribbon gut had been replaced by scar tissue in autopsies done from three weeks to two months after operation. He has also used the material to plicate muscles in operations for the relief of incontinence of both urine and feces.¹² As a further use for the material, Lowsley has used it as a mattress suture to join the membranous urethra to the urinary bladder following total perineal prostatectomy.¹³

Hawes¹⁴ reports the use of ribbon gut in the repair of 26 herniae. However, as two of the 26 had very early recurrences (one in three weeks and one in eight months), and as all of the herniae, except one, were of a very simple type, his results cannot be considered remarkable. Stroebe¹⁵ has used ribbon gut for the control of hemorrhage in operations on horseshoe kidneys. Chanis¹⁶ has recently reported the use of the material in operations for the suspension of the uterus.

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942

All of the above-mentioned users of ribbon gut used chromic gut, and chromic gut was also used in the experiments reported herein

Due to the known tendency of catgut to be absorbed (Lowsley states⁸ that the material used by him was absorbed after three weeks), we wondered if preserved fascia lata strips would not serve his purpose better than ribbon catgut. Probably one reason that he did not use it was that ribbon catgut can be made very much longer than it is possible to get lengths of ox fascia strips. The longest ox fascia strips obtainable are only about 12 inches long. However, the strips can be easily spliced, and in that manner made as long as necessary. Lowsley gives as one of the principal reasons for using ribbon gut the fact that it does not cut through. The same thing, of course, applies to fascia strips.

The excellent results obtained by Lowsley speak well for his skill as a surgeon, but one wonders if his results might not have been even better if he had used a suture material that was not only not absorbable, but had the same qualities as ribbon gut in not cutting through. Very likely, the ribbon gut, in a great many cases during the processes of absorption, was replaced by other fibrous tissue. This is what undoubtedly occurred when bands of ribbon gut were used to encircle the urethra. This process is not new, but is not constant enough to be reliable. Many years ago Lister,¹⁷ Maicy,¹⁸ and more recently Sir Charles Ballance¹⁹ observed the process of substitution and replacement in animal sutures (plain and chromicized catgut and peritoneal or ligatures) by tissues of the host, so that the substituted tissues took the same form as the original suture. Everyone knows that this does not always occur, as in most instances, after a short time, no trace of the original animal suture can be found. Replacement similar to that mentioned above has also been shown experimentally in chromicized kangaroo tendon. In his experiments on this suture material, reported in 1932, Koontz⁶ used heavy kangaroo tendon to suture the sheath of the rectus muscle. Fourteen months later, in one instance, on casual observation it looked as if the original suture were still intact. However, on further investigation, it was found that the groove which the original suture had occupied in the sheath of the rectus was still present and filled with loose areolar tissue. Microscopic examination showed no trace of the original kangaroo tendon. In another similar case, the same condition was found four months after operation.

We believe that it will generally be agreed that in most cases such sutures as those mentioned in the preceding paragraph will be absorbed, and further that in the few cases in which there is some fibrous substitution from the tissues of the host, the fibrous tissues substituted do not have the tensile strength of the original suture. There are, of course, exceptions to all rules.

We conducted some experiments upon dogs in order to determine the differences in the tissue reaction to ribbon gut and ox fascia lata strips. All the experiments were similar. The rectus sheath and muscle were incised on each side and sutured in each instance on the right side with a running stitch of ribbon gut, and on the left side by a running stitch of preserved ox fascia lata. The following are some of the protocols

PROTOCOLS

Experiment 1—March 28, 1940 *Operation* Implantation of ribbon gut and ox fascia lata A right rectus incision was made. The rectus sheath and muscle were divided and sutured with ribbon catgut, continuous suture. The initial end of the suture was tied, while at the terminal end the gut was not tied but fixed through the sheath of the rectus with fine black silk after making one lock stitch. The subcutaneous tissue and skin were closed with medium black silk continuous.

A left rectus incision was then made. The rectus sheath and muscle were divided and sutured with preserved ox fascia lata*. The subcutaneous tissue and skin were closed with medium black silk continuous.

April 12, 1940 Dog died (15 days after operation). Had had distemper for last few days prior to death. On examining the operative site, there was an obvious bulging on the left side, which was fluctuant and contained fluid. On opening this, a good deal of bloody fluid ran out, and the subcutaneous tissues were edematous and contained oily bubbles. The ox fascia was intact and not macerated in any way, but there was maceration of the tissues into which it was sewed. It pulled out, therefore, rather easily. Opening the right side showed the subcutaneous tissue to be edematous also, but there was no fluid collection. Most of the ribbon gut had disappeared, and in places there were some pieces of it left, which appeared like tissue paper. The initial knot was still present. Smear from both wounds showed pus cells but no bacteria.



FIG 1—Photomicrograph showing organization of ox fascia lata with surrounding tissues. Four weeks after operation (Experiment 2) (X25)

Experiment 2—April 4, 1940 *Operation* Implantation of ribbon gut and ox fascia lata. The rectus sheath and muscle were divided on each side as before and on the right side they were sutured with ribbon gut, continuous suture, the initial end being anchored in the same manner as the fascia lata instead of tied. The terminal end was fixed with a lock stitch, reinforced with interrupted fine black silk sutures.

The left rectus was sutured in the usual manner with preserved ox fascia lata.

May 2, 1940 Dog killed (four weeks after operation). The sites of both operations were nicely healed without any evidence of infection or untoward reaction. The ox fascia lata was nicely healed in and organized with the surrounding tissue (Fig 1). The ribbon gut was not absorbed and not organized at all with the other tissues, lying in place as an inert foreign body, and more or less friable (Fig 2).

Experiment 4—April 18, 1940 *Operation* Implantation of ribbon gut and ox fascia lata. The implantation made just as in previous operations except that the ox fascia lata was implanted first, in order to be sure not to contaminate it with preserving solution from the ribbon gut.

June 26, 1940 Dog killed (69 days after operation). None of the ribbon gut could be discovered except the knot at the upper end of the incision. This knot was removed for section (Fig 3). The continuous suture of ox fascia lata was plainly visible on the left side, nicely healed in without untoward reaction.

Experiment 5—May 2, 1940 *Operation* Implantation of ribbon gut and ox fascia lata. The implantation made just as in Experiment 4, implanting the ox fascia lata first and the ribbon gut second.

* The material used in these experiments was all commercially prepared (Johnson and Johnson). The preserving fluid is 1 per cent biniodide of mercury in alcohol. Before using this material it should always be washed thoroughly in two successive basins of sterile salt solution, and then let stand in salt solution until ready for use. A good plan is to have the scrub nurse break the tubes and wash the fascia strips as soon as she is scrubbed up, so that they will have sufficient time to soak before the operator is ready for them.



FIG 2 —Photomicrograph of ribbon gut, four weeks after operation. No organization with surrounding tissues. Gut easily pulled out (Experiment 2) (X25)

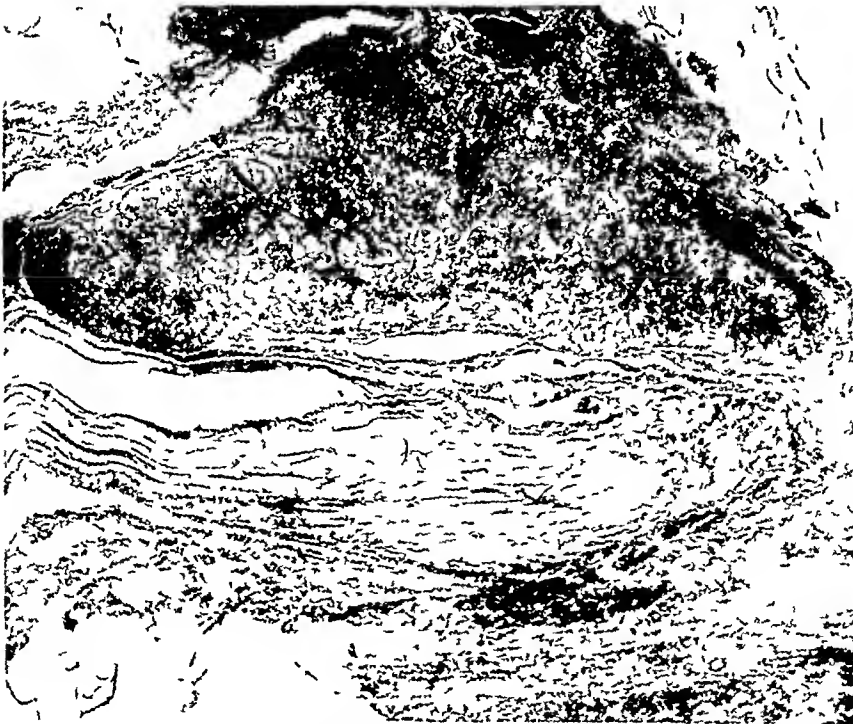


FIG 3 —Section through ribbon gut. Sixty nine days after operation. Gut surrounded by sterile abscess (Experiment 4) (X25)

June 26 1940 Dog killed (55 days after operation) There was a stitch abscess on the right side which, however, did not penetrate below the subcutaneous tissue No trace of the ribbon gut could be seen On the left side, the continuous suture of ox fascia lata was plainly visible and nicely healed in

Experiment 6—May 9, 1940 Operation Implantation of ribbon gut and ox fascia lata The operation performed just as in Experiment 5, implanting the ox fascia on the left first, and then the ribbon gut on the right

FIG 4



FIG 5

FIG 4—Photomicrograph of ox fascia lata Three weeks after operation Fibroblasts of host growing in between the collagen fibrils of the ox fascia lata (Experiment 6) (X100)

FIG 5—Photomicrograph of ribbon gut Three weeks after operation No organization but gut encysted and surrounded by leukocytic reaction (Experiment 6) (X25)

May 30 1940 Dog killed (three weeks after operation) Both sides were nicely healed The ox fascia was well organized in with the other tissues (Fig 4) Fibroblasts were found invading the fascia In the case of the ribbon gut all healing was complete but there was no organization of the ribbon gut in with the other tissues Cross section showed it to be partially absorbed but totally encysted and it could be pulled out readily from the encysting tissues (Fig 5)

The results obtained with the ribbon gut are, therefore, very similar to those obtained with ordinary catgut This is what one would expect Doubtless, the chemicals with which catgut is treated in preparation have something to do with its absorption Also, it is heated in the process of preparation,

which alters the physical state of the collagen fibrils. No such chemical or physical alteration takes place in the collagen fibrils of the preserved fascia strips. Besides, the strips are soft and pliable, and lend themselves readily to the ingrowth of fibroblasts from the surrounding tissues, while catgut is so hardened that it would be impossible for fibroblasts from the surrounding tissues to grow into it, even if there were no question of a complicating physical and chemical alteration of the fibrous framework.

CONCLUSIONS

Strips of preserved ox fascia lata offer the same advantages as ribbon catgut as a suture material in not cutting through, while they present the additional advantages of not being absorbed, and, by virtue of the invasion of fibroblasts from surrounding tissues, persisting as living sutures with an apparently undiminished tensile strength.

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EFFECT OF ORCHIECTOMY AND IRRADIATION ON CANCER OF THE PROSTATE*

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THE RELATIONSHIP OF FUNCTION of certain endocrine glands to prostatic carcinoma was first demonstrated by Huggins and Hodges⁶ who showed that this cancer is frequently inhibited by eliminating the testicular androgens by bilateral orchiectomy or by neutralization of androgenic activity by estrogen administration, conversely, cancer of the prostate is activated by injection of androgens. Subsequently, the favorable action of estrogens in prostatic cancer was confirmed by Herbst³ who reported that estradiol and diethylstilbestrol—the estrogens used by Huggins and Hodges—are substances which “seem to relieve pain due to local prostatic malignant tissue and bony metastatic carcinoma.” Huggins, Stevens, and Hodges⁸ showed that prostatic carcinoma is an abnormal growth of cells resembling adult prostatic epithelium rather than tissue of a more primitive nature. These cancers responded to modifications of the androgenic hormonal status like adult prostatic epithelium such as the cystic hyperplasia of the prostate of senile dogs which increases and decreases in size and function corresponding to changes in the androgenic activity as was shown by Huggins and Clark.⁵

In line with the work cited is the observation of Munger⁹ who treated 11 patients with prostatic cancer by transurethral resection of the prostate, irradiation of the prostatic area (several mapped-out areas were treated until usually each had received 2,000 roentgen units) and irradiation of each testicle (500 r). Munger stated “A study of several cases treated by testicular irradiation with resection seems to indicate that slightly better results were obtained than in those cases treated by resection and roentgenotherapy exclusive of the testicular application.”

It is the purpose of the present paper to survey the course and the results of treatment by surgical excision of the testes alone, and evidence is presented that irradiation of the testes in two cases did not eliminate the interstitial issue of the testes.

MATERIAL—In most instances after opening the tunica vaginalis, the testis was dissected away from the epididymis, followed by closure of the tunica and skin in layers, without drainage. This achieves cosmetic and psychological effects in that two masses of tissue remain in the scrotum.

During the last 30 months, 45 patients with advanced prostatic carcinoma accompanied by local infiltration or metastases have been treated in this clinic.

* Read before the American Surgical Association, Cleveland, Ohio, April 6-8, 1942.

† This investigation was aided by a grant from the Committee for Research in Problems of Sex, the National Research Council.

ORCHIECTOMY FOR CANCER OF PROSTATE

by orchiectomy, 32 of these men had metastases demonstrable on roentgenologic examination of the bones, 21 patients were operated upon more than one year ago, and 15 men in this group had osseous metastases. Roentgenotherapy was employed in no case in this clinic.

RESULTS OF ORCHIECTOMY FOR PROSTATIC CANCER

In the entire series of 45 patients subjected to orchiectomy, there have been eight deaths, all in men with extensive metastases to bone (Table I).

FIG 1



FIG 2

FIG 3

FIG 1—(Hospital No 62292) Adenocarcinoma of prostate with extensive metastases to pelvis, pre-operative roentgenogram

FIG 2—(Hospital No 62292) The same patient as in Figure 1, 201 days after orchiectomy

FIG 3—(Hospital No 62292) The same patient as in Figures 1 and 2, 467 days after orchiectomy, showing complete disappearance of the radiographic evidence of metastases

In four of these men, carcinomatosis was the principal cause of death, while in the others it was of secondary importance. From a clinical standpoint, 31 men have had a sustained improvement lasting as long as 30 months, nine men have had a temporary improvement followed by recurrence of symptoms, and in five men there was no improvement following castration.

In 11 men of the group of 21 patients operated upon 12–30 months ago, there has been significant improvement; these patients are free from symp-

TABLE I

MORTALITY FOLLOWING ORCHIECTOMY FOR PROSTATIC CANCER

45 Patients Treated in 30 Months

	Initials	Hospital Unit No	Age Years	Weight of Testes		Histologic Nature of Neoplasm	Time Since Orchiectomy Days	Apparent Cause of Death
				Gm				
(1)	F F	274090	70	18	18	Adenocarcinoma	4	Pulmonary embolism
(2)	J W G	26645	67	10	10 3		9	Pulmonary embolism
(3)	C R	49318	74	18	20 6	Undifferentiated carcinoma	10	Pneumonia Pyogenic arthritis of knee
(4)	O A	252777	75	12 7	18 1	Adenocarcinoma	53	Cerebral apoplexy
(5)	S R	241797	72	0 7	10 2	Undifferentiated carcinoma	193	Lobarpneumonia
(6)	G P	246583	73	9 0	8 2	Undifferentiated carcinoma	234	Carcinomatosis
(7)	P M	256818	56	13 4	17 0	Undifferentiated carcinoma	332	Carcinomatosis
(8)	M M	247587	57	8 6	7 8		500	Carcinomatosis



FIG 4—M C (a patient of Dr W S Grant) Metastatic adenocarcinoma of the prostate in inguinal nodes on the left the same region 107 days after orchietomy is shown on the right

toms, acid and alkaline phosphatase values of serum are in or near the normal range, there has been complete or partial resolution of roentgenographic evidence of osseous metastases, and a great decrease in size and in the stony consistency of the primary neoplasm on rectal examination. In four patients, extensive osseous metastases have completely disappeared, as determined roentgenographically (Figs 1, 2 and 3).

Thus, it is clear that there are many failures in the treatment of prostatic cancer by orchietomy.

THE "FAILURE CASES" FOLLOWING ORCHIECTOMY FOR PROSTATIC CANCER

The following observations were made in those patients in whom orchietomy did not produce marked resolution of the neoplasm or in whom clinical improvement was not long sustained.

(1) *The Histologic Nature of the Tumor*—Sections of the prostate gland were studied in 16 patients and it was found that a correlation could be made

with the clinical course following orchiectomy. Cytologically, the tumors were classified into two groups: (a) Adenocarcinoma where the tumor formed acini (Fig 5). All of these tumors were in Grades II or III. (b) Undifferentiated carcinoma where tubular structure was not fabricated but the tumor presented solid masses of malignant cells (Fig 7). The clinical course following orchiectomy could be related easily to the cellular pattern. Without exception the tumor was undifferentiated in all of those patients who died from carcinoma, while it was adenocarcinoma in those patients whose course was satisfactory (Figs 4-6). Classification of the tumors into adenocarcinoma and undifferentiated carcinoma, therefore, seems to have meaning although the types interdigitate. Both undifferentiated carcinoma and adenocarcinoma contained large amounts of acid phosphatase and are regarded as

FIG 5

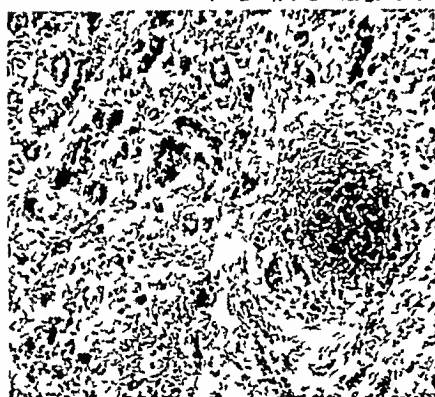


FIG 6

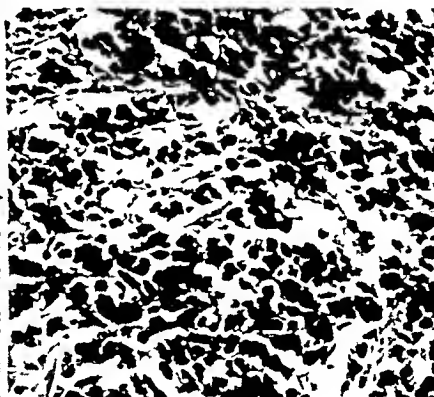


FIG 7

FIG 5—M. C. Metastatic prostatic adenocarcinoma, Grade II in inguinal lymph node before orchiectomy.

FIG 6—M. C. An inguinal lymph node 107 days following bilateral orchiectomy. There has been a marked decrease in the size of the acini which contain little or no secretion and an increase of connective tissue stroma. There are areas of connective tissue scarring containing slits occupied by pyknotic and fused cellular nuclei.

FIG 7—Undifferentiated carcinoma of the prostate stained by the method of Gomori for acid phosphatase.

cancers of adult prostatic epithelium, since the formation of large amounts of acid phosphatase in the prostate is a secondary sex characteristic of a chemical nature. For purposes of prognosis, it is impossible to distinguish between them by studying the serum phosphatases since both may cause elevation of acid phosphatase when they have metastasized.

(2) *The Size of the Testis*—Three of the patients who died of carcinoma had testes which, considered singly, weighed 8–10 Gm at operation. The smallness of the testis is due to a decrease of germinal epithelium, although sheets of Leydig cells remain. The presence of testes, markedly lighter than the normal weight of about 20 Gm, is a bad prognostic sign. Atrophy of germinal epithelium with real or apparent hypertrophy of the interstitial cells is not confined to prostatic cancer. Sand and Okkels¹⁰ observed grave destruction of tubular epithelium in 24 instances in 72 cases of men dying from accidental causes or sterilized by law.

(3) *Decrease of the Primary Neoplasm when the Metastases are Producing a Fatal Carcinomatosis*—It was observed in certain of the failure cases that the primary tumor greatly decreased in size while the metastases were advancing to produce serious illness, such as spinal cord compression (two cases) or even fatal carcinomatosis. This strange phenomenon, in which the hard, and more or less enlarged, prostate gland—at times greatly enlarged—underwent a decrease in size and hardness so that the prostate was completely soft and very small, was observed five times in the presence of the advancing neoplastic process elsewhere in the body. It appears that in certain patients the site of prostatic cancer in bone marrow or lymph nodes as metastasis is more favorable than the original prostatic location, it is possible that adjacent macrophages may facilitate separation of essential foodstuffs, such as androgens, from the body fluids for the improved nutrition of the cancerous metastases.

In other patients in the failure group, slight or no decrease in size of the primary neoplasm occurred, and here the prognosis is bad. Therefore, in advanced prostatic cancer when the primary tumor has undergone marked atrophy, one cannot say merely from atrophy of the primary tumor, as determined by local examination, that the course of the disease is favorable.

(4) *Supplemented Estrogen Administration in Postcastration Failure*—It was shown by Huggins and Clark⁵ that in dogs estrogen administration in adequate dosage masks the stimulating effect on the prostate of injected androgens, it was further demonstrated in this laboratory^{6,7} that estrogen has a beneficial effect at times in prostatic cancer. Accordingly diethylstilbestrol 1–3 mg daily by mouth, was administered to ten patients with advanced prostatic cancer, who had an unsatisfactory response to castration. In one patient, there was a slight reduction of serum acid phosphatase but not to the normal range.⁷ In nine patients, the disease was not perceptibly influenced. It seems that estrogen is able to neutralize to some extent the physiologic properties of the testis androgens, such as testosterone, but not to neutralize the effect of the adrenal androgens. It is believed that estrogen does not usefully supplement orchiectomy in prostatic cancer.

(5) *Hot Flashes A Favorable Prognostic Sign*—The presence of severe hot flashes was seen in all of the cases favorably influenced by orchiectomy, but also in certain of the unfavorable cases. These vasomotor incidents are not believed to be of therapeutic importance but are taken as a sign of androgen-

estrogen deficiency and are usually of favorable prognostic importance. There is no contraindication to their suppression with small doses of estrogen as described by Huggins, Stevens, and Hodges⁸

THE EFFECT OF IRRADIATION OF THE TESTES IN ADVANCED PROSTATIC CANCER

Data were obtained on two patients in whom roentgenotherapy was applied both to the pelvis and testes. The clinical course following irradiation was similar in each.

CASE REPORTS

Case 1—Hospital No 269674 F M, age 47, complained of perineal pain radiating into the right leg, and rectal examination disclosed a large indurated cancer of the prostate, which on biopsy was found to be an adenocarcinoma, Grade II. Four months after the onset of symptoms irradiation was applied to the pelvis over 55 days, according to the following formula: 800 KV, 10 Ma, Filtration, 1 Mm Pb, 1.56 Mm Sn, 2.62 Mm Cu, 3 Mm Al, portals 15×20 cm, tube distance 70 cm, FSD 250 roentgen units, duration of each treatment 7.5 minutes, ten treatments each to anterior and posterior right hip region and ten treatments each to anterior and posterior pelvis. There was symptomatic relief for two months when symptoms recurred and a second series of treatments were given through a 20×30 cm portal, eight treatments to anterior and seven to posterior pelvis, the testes were not screened during the second course of treatments. Relief of symptoms occurred for about six weeks.

Eighty-seven days following the completion of therapy the original symptoms had returned and the patient used canes for walking. On rectal examination, the prostate was nodular, greatly enlarged and of stony consistency, a roentgenogram showed osteoplastic metastases in the right side of the pelvis. Orchiectomy was then performed, the testes weighed 15.7 and 16.3 Gm.

Case 2—H J (ref by Dr C C Moore, Pittsburgh), age 63, complained of pain in the lower back and in the right leg, clinical and biopsy examinations of the prostate gland revealed carcinoma, and there was roentgenographic evidence of metastases in the spine. Roentgenotherapy was administered as follows: In a seven-day period, he received a total dosage of 1,600 roentgen units to each of four portals cross-firing the prostate gland given at the rate of 200 r to each of two anterior portals daily with fields 16×19 cm in size (200 KV constant potential, 0.5 Mm Cu, 2 Mm Al Filtration added). The testes were protected in the usual way with lead rubber but undoubtedly received "back-scattering" of radiation in this series. A second irradiation was given six months later, without lead rubber protection, and the patient received 1,000 roentgen units measured in air, to each of four portals using a field 18×21 cm in size with the application of 100–200 r daily without screening of the testes. The patient failed to improve from this regimen and the prostate gland remained hard and nodular, so that bilateral orchiectomy was performed three months later. The operation was followed by a relief of symptoms and decrease in the size and consistency of the prostate gland.

The testes in each case presented similar cytologic characteristics, namely, profound atrophy of the germinal epithelium with preservation of Sertoli cells and apparent or real hyperplasia of the Leydig cells (Fig 8).

The histologic appearance of the testis following irradiation in man corresponds to data obtained in experimental animals. Bourg¹ in the immature rat found that 1,000 roentgen units destroyed the seminiferous epithelium, but left interstitial cells intact. Heald, Beard, and Lyons² found in rats that an irradiation dosage of 1,152–4,608 roentgen units left the Leydig cells in a functional condition. Hu and Frazier⁴ subjected rabbits to a series of ex-

posures to 1000 roentgen ray, aggregating 2,268 1000 roentgen units (44 erythema skin doses) over a period of 15 days and produced complete atrophy of the germinal epithelium without interference with the secretory functions of the testes

It is thus apparent that 1000 roentgen ray irradiation, in the amounts stated, is ineffective in destroying the secretory function of the testes and is inadequate as a therapeutic agent in prostatic cancer in man

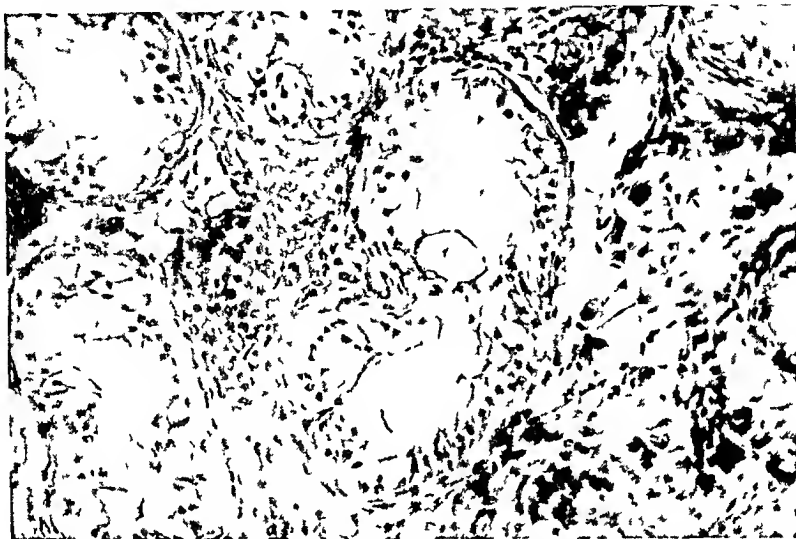


FIG 8—F M (Hospital No 269679) Histologic appearance of the testis 87 days following completion of extensive irradiation with roentgen ray. The dosage is described in the text. Note tubular atrophy with preservation of interstitial cells

SUMMARY AND CONCLUSIONS

In a series of 45 consecutive patients with advanced prostatic cancer, in whom the primary treatment was bilateral orchiectomy, there were eight deaths, all in men with metastasis to bones, in four of these, carcinomatosis was the principal cause of death. In five men, castration caused no clinical improvement, in nine patients there was temporary improvement, and in 31 cases a sustained inhibition of the disease occurred, lasting at least as long as 30 months.

The tumors were classified according to their cytologic appearance into two groups: adenocarcinoma and undifferentiated carcinoma. All of the deaths from carcinomatosis and the patients with no or slight improvement after orchiectomy had undifferentiated carcinoma, while in the more satisfactory cases the cytologic appearance was adenocarcinoma. The findings of testes much lighter than the usual weight of 20 Gm signified a poor prognosis.

A phenomenon of interest, in which a great decrease occurred in the size of the primary neoplasm, while the metastases were advancing, was observed five times in this series.

Estrogen administration was not found to be a useful supplement in the failure cases after orchiectomy.

Roentgen irradiation of the testes in the doses stated, produced atrophy of

the germinal epithelium, but not of the interstitial cells of the testis, and is inadequate as a therapeutic agent in human prostatic cancer

DISCUSSION—DR EVARTS A GRAHAM (St Louis Mo) I rise only because Doctor Phemister asked me to stick my neck out I do not know anything about the prostate of course, but I do want to say that I am delighted to have this work presented here I have been hearing about it I think it is the sort of presentation that the American Surgical Association needs more of

The apology which I made in getting to my feet about the fact that I knew nothing about the prostate was meant to emphasize another point about this Association The Association up until a few years ago was degenerating may I say into an organization which had only so-called general surgeons in it I do not know whether you can degenerate into a general surgeon or not At about that time it was felt desirable that the membership of the Association be leavened somewhat by adding to it some of those men who had gone off into specialties of various kinds Now some of us who went off into thoracic surgery already had our membership in this Association, so nothing could be done about us But an attempt was made to add new life to the Association by adding such people as Doctor Huggins and I think the fact that that was done has been amply justified by his splendid presentation to-day

I think this has another very important bearing and that is to my mind, it represents an approach to the subject to the problem of cancer which is of interest of course to so-called general surgeons the same as to anyone else We are particularly fortunate in having a paper of this sort dealing with the subject of cancer in a broad aspect like this

There are one or two specific points to which I would like to refer Doctor Huggins did not have time to go into the historic aspects of this question, but castration for cancer of the prostate is a very old idea If I am not mistaken I think Bland-Sutton advocated it in the eighties but it was given up, and it has been taken up since then by others and dropped after one or two experiences

It was partly on the basis of the early results obtained in cancer of the prostate after orchietomy that the effort was made to treat cancer of the breast by removal of the ovaries and the same sort of thing has happened again, namely, that after a little experience it has been dropped But there have been sufficiently interesting results accumulated to make this approach at least one of great interest to the study of certain types of cancer

Of course Doctor Huggins has carried the procedure very much farther by applying new knowledge new fundamental knowledge about cancer of the prostate and about the acid and alkaline phosphates to the rationality of the idea of orchietomy But all in all from every possible point of view from which one regards this work one can only commend it to the highest degree

DR ALFRED BLALOCK (Baltimore, Md) As a member of the Program Committee I would like to express our appreciation for this paper and comment on one or two things Doctor Graham has said

In the first place Doctor Huggins was a general surgeon who later developed a particular interest in genito-urinary surgery But the main thing I want to say is this, that he demonstrates in this work I think the value of a prepared mind Doctor Graham made the comment that the testicles were removed in a few instances many years ago for this lesion, but Doctor Huggins came across this because of the fundamental nature of his work in other fields Many of you know of the notable contributions he has made to the study of bone It was because of that information that he was able to grasp the significance of these findings on acid phosphates and to apply them to the treatment of this disease

Having visited in Doctor Phemister's clinic and having seen Doctor Huggins' cases, I can tell those of you who have not seen them that I am sure you will be perfectly amazed

As Doctor Graham has said, if a real contribution is made in cancer in any one field such as Doctor Huggins has made at least it raises our hopes of being able to find out something about cancer in other parts of the body

I think that we as an Association should be very happy in having this excellent work presented here

DR WILLIAM JASON MIXTER (Boston, Mass) I simply wish to say that we have had one such case at the Massachusetts General Hospital that I know of, treated in this way, a case of carcinoma of the prostate with metastasis to the spine, and with very severe pain, that I operated upon for cord compression. Roentgenotherapy did not work very well, and orchiectomy seems to have done a very good piece of work

DR CHARLES HUGGINS (closing) I am highly flattered, and very much embarrassed, by the kind remarks of Doctor Graham and Doctor Blalock. I would like to make just a few comments on the matter of the history of orchiectomy for carcinoma of the prostate. I believe the only person who knowingly, operated to remove the testes for carcinoma of the prostate was Dr Hugh Young, who did this in two patients, with negative results. It is unfortunate that his cases apparently were not of that type which responds well.

The wave of operations that has been mentioned for removal of the testes for prostatic conditions I believe has been confined otherwise to benign prostatic hypertrophy.

With regard to the breast, I am on very uncertain grounds because I think it is extremely unwise to carry over data from one cancer to another cancer. We do know that in the case of the breast this structure is affected by two hormones: one estrogen, from the ovary; the other prolactin from the pituitary. If it is a prolactin tumor, then ovariectomy would obviously be a suitable procedure. I think we have fallen into one error lately and that is to treat patients who are still menstruating with cancer of the breast by roentgenotherapy of the ovaries. Certainly it is impossible to eliminate the interstitial cells of the breast by roentgenotherapy of the ovaries, and I think it is extremely likely that the bad results that are obtained in the breast cancer at the present time by attempting to modify the endocrine state are due to the use of roentgen ray. I strongly feel that surgical ovariectomy should be performed in patients with advanced cancer of the breast with metastasis who are in the menstrual age rather than irradiation.

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